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AUREOMYCIN IN THE TREATMENT OF PRIMARY ATYPICAL PNEUMONIA*

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THE disease generally known as "primary atypical pneumonia" or "viral pneumonia" is now well established as a clinical entity. The fully developed case can usually be recognized by the nature and course of the symptoms, the character of the physical and roentgenographic findings in the lungs, the absence of sustained leukocytosis and the failure to find significant pathogenic bacteria in the blood, sputum or lungs or to obtain clinical cures with the available antibacterial agents. Confirmation of the diagnosis is obtained in a large proportion of cases by the demonstration of cold agglutinins in the patients' blood late in the acute disease or during convalescence.

The ambiguous status of the etiology of this disease is still well characterized by the designation recommended early in the war by the Army Epidemiological Board, namely, "primary atypical pneumonia, etiology unknown."[1] The viral nature of the etiologic agent is strongly suggested by the transmissibility of the disease to normal human subjects by means of bacteriologically sterile filtrates of sputum from active cases.[2] The only viral agent transmissible to laboratory animals that seems to fulfill the criteria for the etiology of this disease is that of Eaton,[3] but his findings still await confirmation by other workers. Furthermore, the finding of certain strains of nonhemolytic streptococci in cultures of lungs and sputum of a number of cases of this disease and the demonstration of agglutinins for these streptococci during convalescence in a significant proportion of cases suggest a possible synergism of such bacteria and some unknown virus in the causation of the disease.[4] There is also the possibility and even likelihood that several distinct nonbacterial agents, as yet undiscovered, produce the same clinical picture.

Irrespective of its etiology, it is generally agreed that there is no definitive therapy for this disease entity. All workers agree that the sulfonamides and penicillin are entirely ineffective in primary atypical pneumonia except possibly so far as they may influence bacterial complications, and even the evidence for the occurrence of such complications in any appreciable number of cases is quite meager. Although streptomycin is also usually included among the antibacterial agents that are said to be without effect on this disease, published reports of its use under controlled conditions in any significant number of cases could not be found.¶ Convalescent serum does not offer a practical therapeutic approach, and even the favorable reports of its use are not entirely convincing.

The discovery of aureomycin,[6] an antibiotic agent that is highly effective against infections with all the known rickettsias and the viruses of the psittacosis-lymphogranuloma-venereum group in animals and in such human cases as there has been opportunity to observe to date, is of particular interest in relation to primary atypical pneumonia. The manifestations of human infections with psittacosis and Q fever are virtually indistinguishable from those of primary atypical pneumonia in which the etiologic role of these or any other known agents can be ruled out. Moreover, other rickettsias, such as those causing epidemic typhus, which are not usually thought of as causes of pneumonia, may produce symptoms and pulmonary lesions that are indistinguishable from those of primary atypical pneumonia except by specific serologic tests or by isolation of the rickettsia. It seems quite possible, therefore, that some as yet undiscovered agent or agents of one of these groups cause some of the cases now classified as primary atypical pneumonia, etiology unknown.

At any rate, it seemed quite reasonable to attempt empirically to determine whether aureomycin would favorably influence the course of this disease. Furthermore, the wide "valence" of the activity

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¶In a cursory review of the literature dealing with either streptomycin or primary atypical pneumonia, direct reference was found to only 2 cases, and in both of them the streptomycin had no effect on the course of the disease.[5]

of aureomycin and its relatively low toxicity served to minimize the hazards of a clinical trial with this agent, since it has been found to be effective both in vitro and in vivo against a large variety of gram-positive and gram-negative bacteria, including those that are commonly found as causes of pneumonia.[6] A preliminary clinical trial in a few cases of pneumococcal pneumonia yielded results comparable with those obtained in similar cases treated with sulfadiazine or penicillin.[7]

It is the purpose of this paper to present and discuss some observations made in the course of the clinical evaluation of the effects of aureomycin in a few selected cases of primary atypical pneumonia. The cases are presented from the point of view of the critical interpretation of these observations rather than in any attempt to arrive at a definitive conclusion concerning the actual effectiveness of aureomycin in this disease. The latter must await experiences with a considerably larger number of cases.

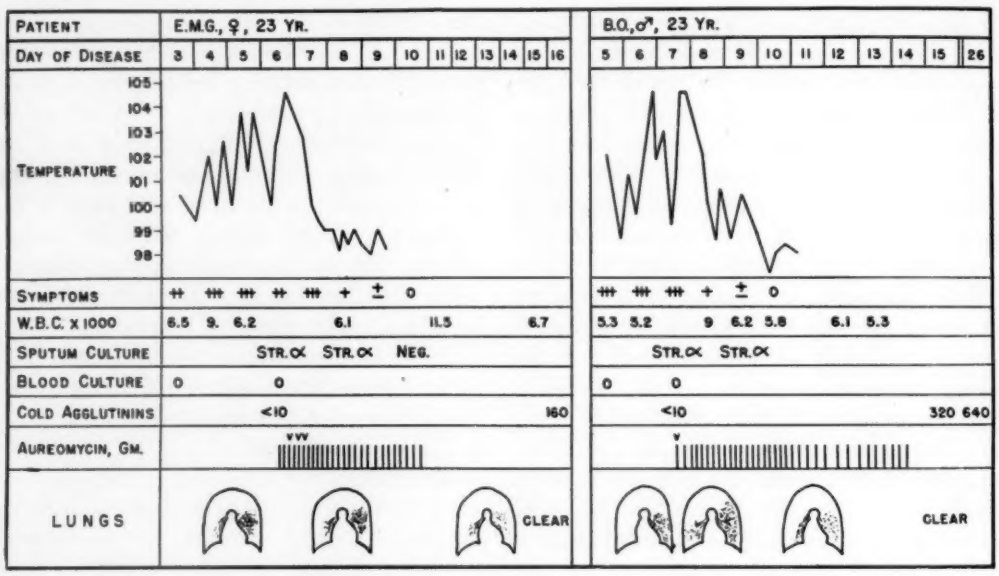


FIGURE 1. *Primary Atypical Pneumonia Treated with Aureomycin by Mouth.*

MATERIALS AND METHODS

Selection of Cases

The patients included here were all young adults either from the various medical services of the Boston City Hospital or from other nearby hospitals where they were observed and the data obtained through the courtesy of their attending physicians.

On the assumption that the great majority of cases of primary atypical pneumonia are quite mild and offer considerable difficulty in interpretation of the effects of the trial agents, it was decided to consider for aureomycin treatment only cases of at least moderate severity in which the clinical and x-ray picture was clearly defined and the patient was acutely ill at the time. When the patient was first seen, the duration of symptoms of the disease was estimated as nearly as possible. This was not always a simple matter because of the occurrence of upper respiratory symptoms before or during the illness and the relation of these symptoms to the pulmonary infection could not be readily assessed. When there was any reason to suspect that the acute disease was receding, as evidenced by recent improvement in the general appearance of the patient or in the fever or symptoms, the patient was first observed for a few hours. The aureomycin was then given only if the temperature rose again and the symptoms returned to the previous severity or got worse, and the antibiotic was withheld if the improvement continued. If other drugs or antibiotics had been used, this delay afforded additional time for evaluation of their effects.

Laboratory Studies

The usual laboratory data, including blood and sputum cultures and white-cell counts, were obtained. In addition, blood was taken for estimation of the cold-agglutinin titers and for other serologic tests before treatment was started and again at suitable intervals.

Dosage

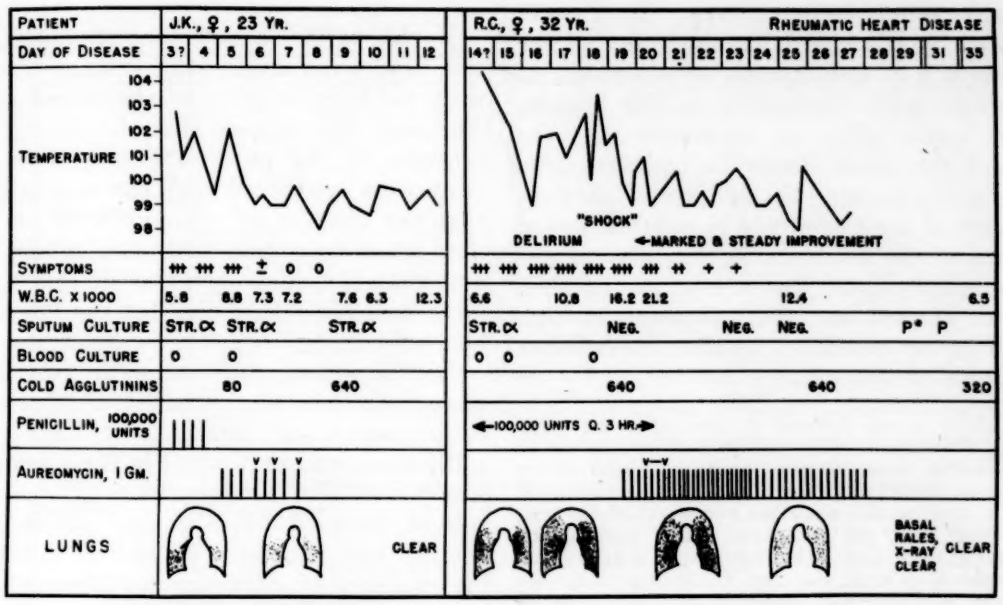
All the aureomycin was given by mouth in the form of capsules of the crystalline hydrochloride. The dosage used was 1 gm. every four to six hours until the temperature had become essentially nor-

mal for a few hours and every six to eight hours for an additional two or three days. The less frequent doses were usually employed in patients who exhibited nausea or vomiting. This dosage was chosen arbitrarily and no attempt has been made, as yet, to determine the optimum dose.

Clinical Results

All the patients included in this study had the classic clinical and laboratory findings of primary atypical pneumonia. The onset was rather insidious, with chills or chilly sensations, and these were followed by increasing malaise, rather severe generalized headache, prostration, irritating cough, which was either dry or productive of scanty yellowish mucoid sputum, and soreness of the anterior portion of the chest and costal margins but no true pleuritic pain. In most cases there was only slight if any dyspnea or cyanosis when the patient was at rest, but these symptoms were present or became accentuated on very slight exertion. There was only slight or moderate dullness to percussion over some parts of the lungs, with only minor or transient changes in the breath sounds or the whispered and spoken voice, but in every case there were large areas of the chest over which showers of medium crepitant rales were heard. Roentgenograms showed the characteristic soft nodular shadows scattered through extensive areas of the lungs, and some also showed patchy areas of partial atelectasis. The white-cell counts were essentially normal except for slight and transient leukocytosis in some cases. Blood cultures were all negative, and cultures of the sputum yielded only the common mouth organisms, *Streptococcus viridans* usually predominating. Significantly high cold-agglutinin titers, usually 1:160 or higher, were attained in the serum at the proper time in every case.

The number of patients who have been treated with aureomycin to date is too small for any statistical evaluation. In every case, however, the temperature fell to and stayed at normal levels within twelve to thirty-six hours of the first dose, and this was accompanied by a loss in "toxicity" and improvement in the systemic and respiratory symptoms, without further demonstrable extension of the pulmonary lesions and with evidence of progressive clearing of the lungs thereafter. Nausea — with or without vomiting, which seemed to occur quite frequently with some of the lots of aureomycin given in large doses — seemed to obscure the early symptomatic improvement in some of the patients, but this usually subsided as recovery set in even though the administration of the antibiotic was continued. The findings are best illustrated by a brief résumé of the first 4 cases in which the aureomycin was used. Some of the more relevant data in these cases are shown in Figures 1 and 2.



*P= Overgrown By Proteus.

Figure 2. *Primary Atypical Pneumonia Treated with Aureomycin by Mouth.*

E. M. G. (Fig. 1) was first considered for aureomycin therapy on the 6th day of illness. There had been downward swings in the temperature on that day and on previous days, but each of these had occurred in response to the administration of aspirin and each was followed by rises to or above the previous peaks with aggravation of the headache and systemic symptoms. Aureomycin was started during an upward swing in fever, and no further aspirin was given. The temperature reached normal and

remained so within 18 hours. Symptomatically, the patient complained of marked nausea, and she vomited three of the doses during the first 24 hours. She improved steadily thereafter, and the nausea and vomiting subsided in spite of the fact that aureomycin was continued for 3 more days. The lungs began to clear promptly and were entirely clear by physical and x-ray examination a week after the antibiotic had been started.

The course of events in B. O. (Fig. 1) was quite similar. Some of the downward swings in temperature followed the taking of aspirin, and others followed alcohol sponge baths. Aureomycin was first given on the 7th day of illness when the temperature was again rising and the lesion in the lung was apparently spreading. This patient vomited once after the first dose, but the temperature dropped precipitately and he was markedly improved within 24 hours of the first dose. The signs in the lungs began to clear in the next 2 days and were entirely clear within 1 week.

Neither of these patients received any other antibiotics or any sulfonamide therapy. Both were essentially well by the eighth or ninth day of the disease. Inasmuch as spontaneous improvement at that time occurs quite frequently in this disease, it cannot be stated with any assurance that the termination of the acute illness in these patients was caused by the aureomycin in spite of the fact that the course of the symptoms in relation to the administration of the antibiotic is strongly suggestive. The absence of cold agglutinins at the time treatment was started and their presence in high titer later may be taken as additional evidence favoring such an interpretation.

In J. K. (Fig. 2) it was difficult to determine the exact duration of the pneumonia. This patient had had an upper respiratory infection with coryza, headache, mild fever and slight nonproductive cough for 2 weeks before she came to the hospital. During this time she had slight chilly sensations and sweats, but she had been taking aspirin frequently and was able to stay at her work until 2 days prior to admission. At that time she had a shaking chill, followed by a severe headache and exacerbation of the previous symptoms with more frequent and severe paroxysmal cough productive of greenish and occasionally blood-tinged sputum. She was given sulfadiazine by a physician, but the symptoms grew steadily worse. She became nauseated and vomited. She was then referred to the hospital, where she remained acutely ill for 2 more days under penicillin therapy. On the 3rd hospital day, when the temperature was again rising, she was started on aureomycin. The fever and symptoms began to improve promptly and she was afebrile and her systemic symptoms had largely subsided in less than 24 hours after the first dose. This patient had some nausea, and she vomited three of the doses on the 2nd and 3rd days and the drug was then discontinued. The lungs began to clear at this time and were entirely clear by physical and x-ray examination 1 week later.

In this case, again, the prompt improvement that followed the administration of aureomycin strongly suggested a causal relation. The finding of an elevated cold-agglutinin titer when this treatment was started, even though the titer later rose significantly, suggests that the disease was of two weeks' rather than five days' duration at that time. The possibility of a normal termination of the acute illness coincidental with the start of aureomycin therapy must, therefore, be considered.

The course of events in R. C. (Fig. 2) again strongly suggests a remarkable and prompt effect from aureomycin, but a critical evaluation of all the data likewise raises considerable doubt. This patient, who was known to have had rheumatic heart disease for at least 7 years, had been ill at home for 2 weeks with chills and fever and a hacking cough productive of yellow and occasionally "frothy, pink" sputum. During this time she was treated with sulfadiazine, but she became much worse 2 or 3 days prior to entry, when she was thought to have cardiac failure and so was sent to the hospital. The symptoms and signs in the lungs at the time of admission were consistent with either diffuse pulmonary congestion or extensive pneumonia, or both. She failed to respond to cardiac therapy and to large doses of penicillin and became confused and disoriented, dyspneic and cyanotic and finally appeared to be in "shock." On the 6th hospital day while in this condition she was started on aureomycin. All the symptoms showed perceptible improvement 18 hours after this therapy had been started and within the next 2 days she was remarkably improved so that her appetite returned and she breathed much more comfortably. The lungs began to clear rapidly, and she was free of all symptoms by the end of the 1st week. Except for a few basal rales the lungs were entirely clear after 2 weeks.

In this patient a high titer of cold agglutinins at the time aureomycin was started was consistent with the long duration of the illness at that time. Although this suggests that the recovery was spontaneous, all the physicians who observed the patient were convinced that she was failing rapidly, that her chances of recovery were very slight indeed when treatment with aureomycin was started and that the administration of this agent was in large measure responsible for the beginning of her recovery.

In the other patients with primary atypical pneumonia who were treated with aureomycin the course before and after this treatment was essentially similar to that noted in the cases cited above. There was also similar difficulty in assessing the role of the aureomycin in each patient, in spite of the fact that they were all acutely ill and not showing evidence of improvement when administration of this antibiotic was started.

During the period when these cases were being observed, however, a considerably larger number of patients with similar clinical findings were seen but in them aureomycin treatment was withheld. These patients differed from the first group only in that, either subjectively or objectively, they seemed to be improving sufficiently to suggest that they were approaching the termination of their acute illness although they were still febrile and moderately ill when they were first considered for aureomycin therapy. In almost every case the subsequent clinical course was in every way similar to that of the 3 cases cited above, in spite of the fact that aureomycin was not used. Two of these cases are of particular interest because the findings suggest that clinical improvement occurred in response to the administration of streptomycin. Some of the relevant findings in these 2 cases are shown in Figure 3.

I. M. was first seen with a view to aureomycin therapy on the day after admission to another hospital. It was the 6th day of illness, and the symptoms were becoming progressively worse. She had received injections of 300,000 units of procaine penicillin in oil on each of the 2 days preceding admission, and this had been discontinued. She was

then started on injections of 0.5 gm. of streptomycin every 6 hours and when first seen she had already received four such injections. During the 4 hours immediately preceding this visit the temperature had dropped appreciably, she was free of headache, and the malaise had eased considerably for the first time without antipyretics or analgesics. The streptomycin was continued for another 36 hours, during which she became entirely afebrile and symptom free and the lungs began to clear rapidly. Further injections of aqueous penicillin were given by a physician "to prevent secondary bacterial infection" while she remained in the hospital.

S. S. had a more severe illness and more extensive pulmonary involvement when he was first seen by one of us at a hospital in another city. It was the 9th day of illness, and he had received moderately large doses of penicillin during the previous week and these doses had been increased on that day. In addition, at the end of the 7th day, when the temperature reached 104.8°F., the pulmonary lesion had spread and the patient appeared to be getting much worse, he was started on injections of streptomycin (0.5 gm. every 4 hours). He had already received a total of 5 gm. at the time when he was seen. It was then apparent from his temperature chart that his fever was receding gradually but steadily, and, although he was still moderately ill, slightly cyanotic and sweating profusely, he readily admitted that he had been improving steadily in every respect during the preceding day. Aureomycin was, therefore, withheld, and, under further observation, he continued to improve steadily and his lungs began to show signs of clearing during the next 2 or 3 days.

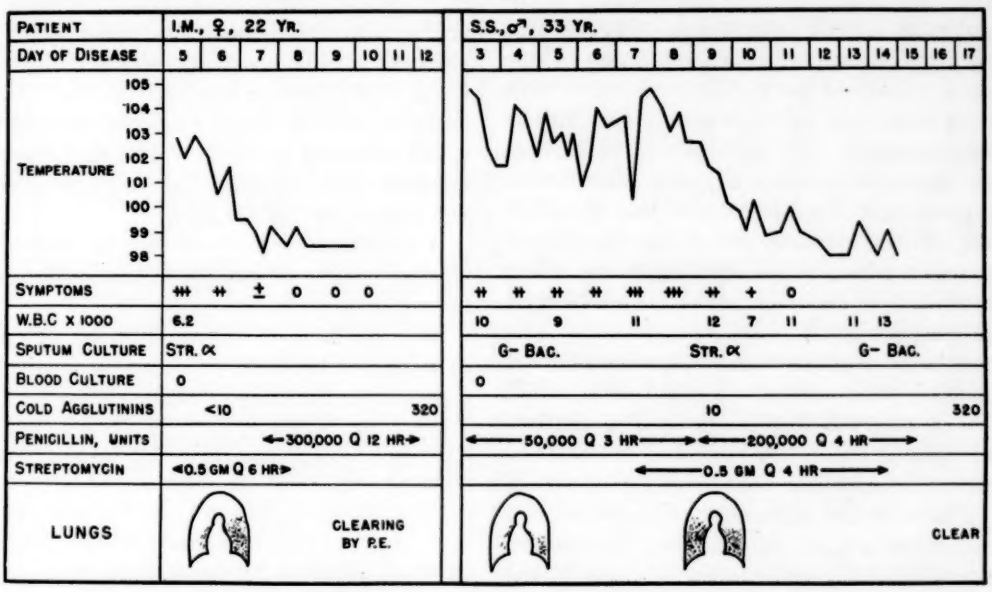


FIGURE 3. *Primary Atypical Pneumonia Treated with Penicillin and Streptomycin.*

The acute febrile illness terminated on the seventh day in I. M. and on the tenth or eleventh day in S. S. In both patients, as in the 2 cases shown in Figure 1, there were no cold agglutinins in the serum when aureomycin therapy was first considered, and high titers appeared in later specimens in each case. The effect of streptomycin in these 2 patients obviously cannot be assessed with certainty, but the favorable course following its use at least suggests that this antibiotic had a beneficial effect on the course of their disease.

In an occasional patient the symptoms during the first day or two of observation were relatively mild or seemed to be improving either without specific therapy or while only penicillin was being given. The course of events in a patient in whom penicillin therapy was continued without the addition of either streptomycin or aureomycin may be mentioned. This patient was seen with a view to aureomycin therapy during the low points of his fever on the fourth and fifth days of his illness. On each occasion antipyretics had not been given, and it was believed that the patient might be improving spontaneously so that if aureomycin were started at that time it would not be possible to assess its effects. The course of this patient during the next ten days was characterized by a low-grade fever, severe cough, moderate malaise and headache, with some extension of the pulmonary lesion by physical and x-ray examination. Cold agglutinins, which were absent at first, were present in low titer on the eleventh day and in a much higher titer a week later. This case illustrates the fact that it has not been possible, on the basis of observations made during the first few days of the acute illness, to predict the subsequent course of the disease.

The question then is, How may one arrive at a reasonable estimate of the true value of these apparently effective agents in a disease with so variable a course as primary atypical pneumonia in which the early stages are so ill defined? It seems obvious from the cases presented that if treatment with the trial agents is withheld until the patients show progressively increasing severity of the symptoms or extension of the pulmonary lesions, the use of these agents will be confined essentially to a stage of the disease when the illness may be expected to terminate spontaneously in increasing proportions of cases.

Were all cases to be treated as soon as the diagnosis of primary atypical pneumonia is made or suspected on clinical grounds, the great majority of the patients treated might turn out to have either a disease that is ill defined (undifferentiated acute respiratory disease[8]) or at most a rather mild case of primary atypical pneumonia in which the effects of the agents would be difficult to assess. Proof of the effectiveness of these agents in the cases that proved to be primary atypical pneumonia would, in any event, have to depend on the demonstration of a constant beneficial effect in consecutive cases and in direct relation to the initiation of the treatment. In addition, adequate causes, extraneous to the primary pulmonary infection, would have to be established to account for the failures.

On the other hand, should any appreciable number of such patients show a progression of symptoms and pulmonary lesions under adequate doses of one of these agents, it would be possible to state with some assurance that that agent was not specifically effective in this disease. On the basis of this argument, the few cases of primary atypical pneumonia in which streptomycin is said to have had no effect on the course of the disease are more significant than the 2 cases in which a possible beneficial effect was noted, provided, of course, that the same criteria were used for diagnosis.

The patients with whom we are concerned in the present evaluation were acutely ill and febrile when aureomycin was started, and each had a history and physical examination. X-ray and laboratory findings were characteristic of primary atypical pneumonia. The first 20 consecutive patients who satisfied these criteria and, in addition, developed significant titers of cold agglutinins in their blood at the appropriate time were all markedly improved clinically and were afebrile within twelve to forty-eight hours (the great majority within twenty-four hours) after the first dose of aureomycin was given. The pulmonary lesions then cleared rapidly in every case. On the basis of these consecutive favorable responses, therefore, aureomycin may be said to be highly effective in the treatment of cases of primary atypical pneumonia of the variety that is associated with the development of cold agglutinins. Further details of these cases and the findings in cases of other types of pneumonia that have been treated with aureomycin will be given in a later report.

While this study was in progress, similar studies on the effects of aureomycin in primary atypical pneumonia were being carried out by several other groups of workers. Reports from two of these groups, one from New York[9] and the other from Baltimore,[10] have already appeared. In each instance favorable responses similar to those reported here were noted in consecutive cases of this disease, and in the majority of the cases cold agglutinins were demonstrated at the appropriate time. Both groups of workers are convinced that aureomycin has a definitely favorable effect on this disease.

Summary

A small group of patients with the characteristic clinical, x-ray and laboratory findings of primary atypical pneumonia were treated with aureomycin by mouth. They were all moderately or severely ill when this treatment was started, and their fever and symptoms began to improve promptly and subsided in all cases within twelve to forty-eight hours. Cold agglutinins appeared in high titer late in the acute illness or during convalescence in the serum of all of these patients. The findings in these cases suggest that aureomycin had a favorable effect on the course of the disease.

Two cases are presented in which a somewhat similar course of events followed the administration of streptomycin.

The problem of the evaluation of curative agents in primary atypical pneumonia is discussed in relation to the findings in these cases.

We are indebted to Mildred W. Barnes for carrying out the cold-agglutination tests, and to Clare Wilcox for bacteriologic studies of the sputums.

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OVARIAN NEOPLASMS IN A HERMAPHRODITE*

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HERMAPHRODITISM in itself is a rare anomaly. The additional occurrence of bilateral gonadal neoplasms is exceedingly uncommon. The present paper reports the case of a "male" hermaphrodite with a pseudomucinous cystadenoma of the right ovary and a dysgerminoma (seminoma) of the opposite gonad.

GENERAL CONSIDERATIONS

Hermaphroditism is the term used to designate the congenital possession by one person of both male and female sex organs. Two forms exist, true hermaphroditism and pseudohermaphroditism. Diagnosis of the former requires the presence of both ovary and testis either as separate organs or combined to form unilateral or bilateral ovotestes. In pseudohermaphroditism, on the other hand, the gonads are either ovarian or testicular, and only the secondary sex organs are both male and female.

True hermaphroditism is quite rare, only 38 cases appearing in the literature.[1] Pseudohermaphroditism, in contrast, is stated to occur to some degree in 1 out of every 1000 females; it is considerably less frequent in males.[1]

Tumors occurring in hermaphrodites may arise from ovarian or testicular tissue, in pure organs or in ovotestes; often the gonad is destroyed by the neoplastic process so that the site of origin is impossible to determine.

No neoplasm is found in constant association with hermaphroditism. The most commonly reported one is the dysgerminoma,[2] a highly radiosensitive malignant tumor composed of large, clear epithelial cells growing in diffuse sheets or nests isolated by a stroma rich in lymphocytes. According to Meyer[3] the dysgerminoma is a tumor of the neuter germ cell of the embryo; it arises in ovarian or testicular tissue; in the latter site it is better known by the names, seminoma[4] and embryonal carcinoma.[5] Meyer[3] collected 27 cases of dysgerminoma occurring in hermaphrodites. Five were bilateral. Two of the 27 patients had an ovotestis on the side opposite the tumor.

In addition to hermaphrodites the dysgerminoma tends to occur in persons with less striking sexual abnormalities, including male cryptorchidism and female hypoplasia of the genital organs. The majority of dysgerminomas, however, arise in apparently normal men and women.[6]

Beyond the observation that dysgerminomas are encountered with unusual frequency in persons who approach neutrality in sex, there is no apparent causal relation between dysgerminoma and hermaphroditism, for the latter is a congenital malformation that remains despite removal of the tumor.

A second tumor that has been reported with some frequency in hermaphrodites is the so-called tubular adenoma of the testis.[7] This occurs as single or multiple small nodules in the cryptorchid testicles of both normal and hermaphroditic patients. It appears in most if not all cases to be a nodular hyperplasia in an atrophic, cirrhotic organ rather than a true neoplasm; it has no clinical significance.

One of the most controversial aspects of hermaphroditism is the proper classification of patients with arrhenoblastomas — that is, ovarian neoplasms that resemble testicular tissue and often cause masculinization. These tumors range from tubular adenomas, which may bear a striking resemblance to the so-called adenomas of the cryptorchid testicle, to highly undifferentiated sarcomatoid forms. According to Pick[8] the tubular adenoma arises in the testicular portion of an ovotestis; hence, a person with such a tumor is a hermaphrodite by definition. Meyer,[3] on the other hand, believed that the assumption of the existence of an ovotestis is not necessary since the embryonic rests of testicular tissue present in the normal ovary adequately account for the occasional occurrence of masculine tumors. In support of this is the fact that convincing evidence of congenital hermaphroditism is quite rare in patients with tubular adenomas.[9]

Gonadal neoplasms other than dysgerminoma and testicular adenoma have been reported in small numbers of hermaphrodites.[9, 10] No case of pseudomucinous cystadenoma of the ovary was encountered in an extensive, albeit incomplete, review of the literature.

CASE REPORT

A 38-year-old patient, stated to be a man, who was married but had no children, was admitted to the hospital complaining of pain and discomfort in the abdomen.

The father was living, aged 77. The mother had died in 1927 from leukemia. One sister was living and well; she was married and had 3 children.

At the age of 1½ the patient was in the hospital for some sort of operation on the penis, and at the age of 3 he was confined to the hospital because of trouble with urination. From that time until he was 35 he had absolutely no trouble.

For a year prior to admission to the hospital the patient had been having episodes of pain and discomfort in the abdomen associated with nausea and vomiting. He had been married for 11 years and as far as could be ascertained he had sexual relations with his wife. Four weeks before admission the patient had suffered low-back pain and diarrhea. There were no bloody stools. The pain gradually migrated laterally to the mid-lower abdomen.

The temperature was 99.5°F. by rectum. The blood pressure was 130/70, the pulse 85, and the respirations 20.

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Physical examination revealed a rather short, stocky, slightly obese man weighing about 140 pounds. The patient had a normal beard and a normal distribution of hair over the entire chest. Examination of the abdomen revealed a slight bulge in the right lower quadrant. Palpation disclosed a smooth, round, nontender tumor. The left side of the lower abdomen appeared normal. Examination of the genitalia showed a normal growth of pubic hair, with complete absence of the scrotum. There was a typical hypospadiac penis, which was small (approximately 4 cm. long). The prepuce was not covered with skin. Approximately 4 cm. back from the head of the prepuce there was an opening through which he urinated. There was no opening in the head of the penis. Rectal examination was entirely negative.

A barium enema showed the colon to fill and evacuate well, without evidence of intrinsic disease. A normal-appearing appendix was visualized. There was a discretely outlined oval mass, 11 by 15 cm., displacing the cecum upward. The mass was situated in the right lower hypogastrium and pelvis. The impression was that of a malignant tumor, as noted, originating in an undescended testis. Pyelography was recommended to rule out the lesser possibility of renal tumor.

Intravenous pyelography showed normally draining structures bilaterally. The only abnormality to be seen was a slight extrinsic pressure defect on the right ureter, displacing it medially.

The diagnosis was abdominal tumor, probably testicular in nature. Under continuous spinal anesthesia a long incision was made in the right lower quadrant. When the abdomen was opened a large, round, smooth, thin-walled tumor, apparently ovarian in origin, was found. The tumor, approximately 15 cm. in width, was attached to a small, hard mass, which was posterior to the urinary bladder. Further observation disclosed a large, hard, irregular mass, measuring 8.5 by 7 by 3 cm., in the left pelvis, which was well encapsulated and firm to palpation. The incision was enlarged, and further examination revealed a small, hard, fairly well developed uterus, which ran off into a small tubular structure just beneath the bladder. At this time a sound was passed through the meatus and could be palpated in the urinary bladder. The small tubular structure evidently ended in the peritoneum of the pelvic wall. Both tumors with the tissue attached to them were removed and given to the pathologist. Nothing further was done. The abdomen was closed without incident.

Postoperatively the patient did extremely well except for the 2nd night after operation, when he began to complain of severe hot flashes. He was given stilbestrol, 0.1 mg. nightly. After a few days the hot flashes diminished. He was discharged from the hospital 12 days after the operation and has since been on stilbestrol therapy.

The pathological report was as follows:

> The gross specimen consists of a cyst (from the right pelvic mass) measuring 15 by 13 by 8.5 cm. It is translucent, and when the wall is incised, it is found to contain about 750 cc. of a clear, serous fluid and the cyst is multiloculated. The inner lining of the cyst is smooth. One of the cysts is filled with a chocolate-colored material.
>
> There is an irregular, lobulated mass (from the left side of the pelvis) measuring 8.5 by 7 by 3 cm. It appears well encapsulated and is fairly firm to palpation. On section it is almost solid and is yellow gray. The cut surface is glistening. Attached to one side of this tumor is a tubular structure, which grossly resembles a fallopian tube.
>
> Two sections taken from the cyst of the right gonad show a multilocular, pseudomucinous cystadenoma. The cysts, which vary considerably in size, are surrounded by dense collagenous tissue that bears a striking resemblance to ovarian stroma. The cyst lining varies from a columnar mucus-secreting epithelium to an indifferent squamous one; in some areas the lining cells are piled up; however, there is no evidence of malignancy. Occasional cysts are filled with serous fluid. The stroma surrounding the cysts may be extremely cellular with crowded, plump fibroblasts or may show hyalinization. In the cellular areas cords of epithelioid cells become intimately mixed with the stromal elements. The former are polyhedral and are characterized by distinct cell borders, abundant pale cytoplasm denser centrally, and pale, round, central nuclei; their appearance is suggestive of theca interna cells. The tumor is encapsulated by a layer of dense collagenous tissue resembling tunica albuginea. No testicular or specific ovarian elements (other than stroma) can be identified in the sections. External to the capsule of the tumor is a tubular structure that has the characteristics of the isthmic portion of a fallopian tube.
>
> One section taken from the tumor of the left gonad shows a dysgerminoma characterized by interlacing cords and alveoli of uniform polyhedral cells separated by a collagenous stroma rich in lymphocytes. The cytoplasm of the tumor cells is clear and has a somewhat vacuolated appearance owing to post-mortem degeneration. The nuclei are round to oval, contain heavy granular chromatin and show slight to moderate variation in size and shape. There are occasional mitoses. Small numbers of epithelioid cells and multinucleated giant cells filled with fine fat droplets are present, especially at the periphery of the cords. The tumor is encapsulated by a layer of dense collagenous tissue resembling tunica albuginea. No testicular or ovarian tissue is identifiable.
>
> A final section taken from the tubular structure attached to the left gonadal tumor shows epididymis and a large duct lined by alternating groups of tall and low cells, giving the lumen a festooned circumference, which suggests that the duct is a ductulus efferens of the testis despite its large size.
>
> The diagnoses are dysgerminoma of the left ovary; pseudomucinous cystoma of the right ovary and rudimentary fallopian tube.

Discussion

In summary, this patient had both male and female secondary sexual organs. Was "he" a true hermaphrodite or a female pseudohermaphrodite? There is considerable evidence that the right gonad was an ovary: it was occupied by a pseudomucinous cystadenoma in which the cysts were surrounded by typical ovarian stroma*; pseudomucinous cystadenomas do not, to my knowledge, arise in the male gonad; and there was clinical evidence of estrogen withdrawal postoperatively. It is entirely possible that the cords of epithelioid cells in the stroma were estrogen-producing theca interna cells or that the stroma itself was estrogenic.

The identity of the left gonad presents an insoluble problem; no traces of testicular or ovarian tissue were present in the section of tumor. The tumor itself was consistent with an origin in either testis or ovary. The degree of nuclear hyperchromatism of the neoplastic cells is, in my opinion, a more common feature of the ovarian rather than the testicular dysgerminoma; this evidence, however, is only suggestive. In conclusion, then, it is believed that there is somewhat more evidence that this patient possessed two ovaries, and hence was a female pseudohermaphrodite. This conclusion is given some statistical support by the great rarity of true hermaphroditism.

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RIGHT- OR LEFT-HANDEDNESS*

A Practical Problem

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A PHYSICIAN who is asked if it is safe and wise to train an apparently left-handed child to use pencil and pen with his right hand can find good authority in the literature for almost any answer he may choose to give. The more he studies the subject, the more confusing it becomes. The theories propounded are various and conflicting.

If he then tries to form his own opinion by testing and observing his patients he soon finds that his decision whether a given child is right-handed, left-handed or ambidextrous often depends on the number and type of tests used. If his bias is toward a comparatively large number of ambidextrous subjects, all he need do is administer a large battery of laterality tests that include the relatively unskilled activities. On the other hand, a smaller battery testing chiefly the skilled activities will give less evidence of ambidexterity and more of definite right-handedness or left-handedness. There are many exceptions, but by and large the more tests that are given and the more the untrained activities are included the greater the amount of mixed or confused dominance that will be found.

The problem of handedness is actually a double one, although the duality is ignored by many. The first question is why man alone among primates has developed a preferred hand, and the second is why in approximately 95 per cent of adult, civilized, tool-using peoples the preferred hand is the right.

General Considerations

Although man from most anatomic points of view is a bilaterally symmetrical animal, he is in reality decidedly asymmetrical in function. Attempts have been made to demonstrate this asymmetry in some of the lower animals, such as the rat, horse, dog, monkey and ape. It cannot be denied that some of these at times show a preference for one side over the other, but this vague, indefinite preference is far from the skilled, unilateral handedness shown by the great majority of human adults. Monkeys and apes have developed unilaterality a little farther than the others in that they manipulate an object with one hand while the other is used for support or for holding and steadying, but they seem to have no great preference regarding the hand that does the manipulating. The ability to develop a preferred and hence more skillful hand is a characteristically human trait, which apparently has arisen as an inevitable result of man's one-handed use of tools and weapons. It seems clear that the acquisition of skill in one hand is a gradual process largely dependent upon training through habitual use.

Man's unilateral handedness, however, is fluid, not fixed. What one hand can do the other can also do, although until practiced it is slow, clumsy and awkward. This bimanual ability is exemplified by the skill of the pianist and typist with the ordinarily nonpreferred hand. The fluidity is particularly marked in childhood when the preferred hand is still far from skillful and the nonpreferred hand can do almost as well as the other.

Handedness in Infancy

Handedness in infancy means only the somewhat more frequent use of a particular hand for reaching, touching and eventually grasping objects. This sort of activity is very different from the handedness of an adult, whose habitual use of one hand has greatly increased its skill. In the infant and young child the more frequently used hand shifts from side to side at fairly definite intervals, with periods when both hands are used either together or with no choice between them.[1-5] The studies of Conel[6] suggest that this alternation in use depends upon changes and new connections in the constantly growing association tracts. Whatever the cause may be, the practical result is that both hands receive some training, so that the final outcome is, "not a good hand and a poor one, but a good hand and a better one."[7]

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Unilateral Handedness

At the present time the adult civilized world is approximately 95 per cent right-handed. The origins of this preference for the right are lost in prehistoric antiquity, and no theory accounts satisfactorily for the observed fact. The various hypotheses, some of them almost ludicrous in their simplicity, that attempt to explain it have been well summarized by Wile[8] and Blau.[9] Their reports of the agreed facts on right-handedness and left-handedness may be summed up as follows:

Archeologists have demonstrated that the amount of left-handedness has diminished from the dim past to the present. Implements dating from the Stone Age are reported to show that about 50 per cent were chipped or flaked for left-handed use. Only about 25 per cent of the weapons and tools from the Bronze Age were so fashioned, and at present no more than about 5 per cent of civilized peoples are left-handed.

Anthropologists report that there is more left-handedness among contemporary primitive races than among cultured, tool-using men.

Finally, there is a steady diminution in the frequency of left-handedness from infant to adult. Roughly 20 per cent of kindergarten children, 10 per cent of school children, and only 5 per cent of adults are reported to be left-handed.

Right-Handedness Due to Environmental Pressure

This steady increase of right-handedness with proportionate decrease of left-handedness — from the Stone Age to the present, from living primitives to cultured peoples and from child to adult — is convincing evidence of the importance of environmental pressure in determining ultimate handedness. As stated above, however, no theory accounts satisfactorily for the fact that this pressure is always in favor of the right. Whatever the original reason, the child of the present day has to live in and conform to a right-handed world.

Theoretical Causes of Left-Handedness

Environment alone, however, does not explain the whole picture because it does not account for the persisting existence of a small proportion of left-handed adults. Some believe, without completely convincing proof, that left-handedness is inherited according to the Mendelian law. Others argue that it is acquired as the result of one of the following causes: temporary disablement of the right hand during childhood before the pattern has been firmly set; imitation of left-handed siblings, parents or other adults; deliberate training of a child's left hand by adults who mistakenly believe that because he is using his left hand about as much as his right he is going to be left-handed and help him to become so; and accidental training of the left hand by an adult who when facing a child becomes confused himself between left and right. To these Blau[9] adds childhood negativism, — the urge to act contrary to precept and to the example of the majority, — which he believes is responsible for most left-handedness. His argument is interesting although not wholly convincing and leaves the reader with the impression that negativism may account for some but surely not all left-handedness.

Characteristics of Left-Handedness and Ambidexterity

The presence of left-handed and ambidextrous persons in a predominantly right-handed world has puzzled the curious ever since the days of the invasion and settlement of Palestine by the ancient Hebrews.[10] Although the problem of their persisting existence may seem purely scientific or theoretical, it has its practical aspects as well.

A tendency toward ambidexterity appears to be more important in this connection than left-handedness itself. The strongly right-handed or left-handed person is not particularly prone to "specific" language disturbances,* which occur more frequently among the partly ambidextrous, regardless of whether they use the right hand or the left for most activities. Unusual aptitude with the nonpreferred hand is more common among left-handed than among right-handed people, as is obvious when one considers that all mature sinistrals use the right for shaking hands, many for eating, and some even for writing. Partial ambidexterity, rather than left-handedness itself, thus seems to be the important factor associated with these language disabilities.

Ambidexterity implies a mixed or varying cortical dominance, the left cortex taking the lead in some activities and the right in others. The nerve cells that are active in controlling language are, with rare exceptions, in the left cortex in right-handed and the right cortex in left-handed persons. Unfortunately, the only practical way to locate the functioning language center in normal persons is by inference from the patients' handedness. When that is confused or uncertain one is left in doubt. Orton[11] and others argue that lack of clear cortical dominance is the cause of the specific language disabilities. Although absolute proof of this hypothesis is lacking, it seems very clear that there is some relation between a tendency toward ambidexterity and comparative weakness in the use of language.

Left-handedness and ambidexterity are also more common among children, the mentally retarded, criminals and geniuses. This does not mean that they are causes of these conditions. Children are still in the original state of using both hands fairly equally; the mentally retarded, in this as in most respects, are still children; some criminals fall into

*Motor speech delay, infantile speech, stuttering and specific reading disability are regarded as specific language disabilities.

the same group, whereas others seem to exemplify Blau's theory of a negativistic attitude toward the world; and geniuses by and large are extremely individualistic and hence more likely than the average to resist successfully the external pressures toward right-handedness.

Theories of Left-Handedness and Ambidexterity

Of the many theories propounded to account for the existence of left-handedness and ambidexterity in a right-handed world, none have been widely accepted. In general they repeat with variations the old and endless dispute between the champions of heredity and of environment. Simply stated, the unsolved question is whether right-handedness and left-handedness are inherited as such or are acquired after birth as a result of imitation, training, and social and cultural pressure. In such a complex human skill as unilateral handedness, it seems likely that both factors are usually involved.

Fluidity of Handedness in the Infant and Small Child

Right-handedness and left-handedness in the usual sense of the terms are absent in infancy. A baby has no particular skill with either hand and, as Blau[9] states, should be classed as ambilateral rather than ambidextrous. Giesecke[1] reports that from a few hours after birth one hand is more active than the other and that later this more active hand is the one chosen for reaching and grasping. Gesell[2] has shown that more frequent use of a particular hand for reaching and grasping does not begin until the infant is at least sixteen weeks old. Throughout infancy this more frequent use of one hand should not be taken to mean that it is the dominant or master hand in the adult sense; it indicates merely that it is the preferred hand for the time being.

The truly skilled and leading hand does not appear for several years. In fact, as Giesecke,[1] Gesell[2] and others[3, 4] have demonstrated, the most used hand shifts from side to side at fairly regular intervals for a number of years. Gesell states that an infant passes through definite phases of being right-handed, left-handed and bilateral. He has reported a number of children who were apparently right-handed at two years and equally left-handed at three years, before becoming finally and permanently right-handed at five years. Evidently it is not until habitual use of one hand over a long period has given that hand definitely superior skill that it is fair to describe its possessor as a right-handed or left-handed person.

Unless this normal variation of handedness in infancy and early childhood is kept constantly in mind, laterality tests of young children may be extremely misleading. Certainly no definite or final conclusion about a person's ultimate handedness should ever be drawn from them.

Inheritance as a Cause of Handedness

The influence of environment on handedness has been shown. It seems very certain, however, that this is not the only factor concerned. Some cases of left-handedness and ambidexterity appearing in the same family over several generations may undoubtedly be ascribed to environment. In many others, however, the left-handed relatives were so widely separated in time or space that imitation could not have been responsible for their occurrence. One is therefore forced to admit that inheritance may also play its part in determining the final result.

Until fairly recently those who believed in the inheritance theory were forced to assume something in the genes that led to the eventual dominance of the left or right cerebral cortex and so to right-handedness or left-handedness. Their opponents meanwhile insisted that it was the more frequent use of the preferred hand that established dominance in the appropriate cortex.

A clue to how heredity may affect handedness has been suggested by Gesell.[2] He has traced back into fetal life a basic trend toward the final adult handedness by demonstrating a relation between the preferred tonic-neck-reflex position of the premature infant and his ultimate handedness. Since the tonic neck reflex develops as early as the twenty-eighth week after conception,[12] it seems impossible that environmental pressure after birth can do more than modify a fundamental tendency.

Tonic Neck Reflex of the Human Infant

When a normal newborn infant turns his head to one side, the arm and leg on that side automatically straighten and extend themselves, the opposite arm bends toward the head, and the opposite leg flexes at the hip and knee. Equally automatically, this position reverses itself when the infant turns his head the other way. This obligatory response to the turning of the head is known as the tonic neck reflex.

It is present in typical form in all normal newborn babies, fading gradually and becoming replaced by symmetrical arm and leg movements by the time the infant is twenty weeks old. Its presence at an older age indicates serious disease of the brain.[13]

Neuromuscular Development in the Salamander Embryo

An example taken from a lower form of life is illuminating. Coghill[14] succeeded in correlating the behavior of the amblystoma embryo at different stages of development with the growth of its nervous system. His account is fascinating and too little known among physicians.

At an early stage the embryo lies motionless and does not respond to stimulation. A little later it spontaneously "bends itself into a tight coil . . . [which] may be reversed instantly into a coil in the opposite direction." The flexing motion begins at the head and progresses caudad.

The next stage is the appearance of a second flexion of the head in the opposite direction before the first has reached the tail. These flexions, when better co-ordinated and more rapid, result in forward motion of the embryo, as in swimming. When the forelimbs are sufficiently developed, the one on the concave side is adducted, and the one on the convex side is abducted during flexion of the neck and trunk. These movements are the beginnings of forward motion of the body on land, as in walking.

Coghill demonstrated conclusively that the coordination of these flexions into swimming movements depends upon the growth of connecting cells in the floor of the medulla and in the upper part of the cord: "The growth of terminals of nerve cells over a distance of less than 1/100 of a mm. transforms (the animal) from (one) that must lie helpless where chance has placed it into one that can explore its environment . . . "

Resemblance between Salamander and Infant

There is a striking similarity between Coghill's drawings of amblystoma illustrating the beginning of walking and Gesell's photographs of infants in the tonic-neck-reflex position. The resemblance is so marked that it seems extremely likely that they represent approximately equivalent stages of development of the nervous systems of the two species.

Relation of the Tonic Neck Reflex to Handedness

Gesell[2] reports that the great majority of infants when in the tonic-neck-reflex position spend more time with the head turned to the right than to the left. He followed 10 infants with predominantly right tonic neck reflexes for ten years and found that they all became right-handed children. He followed 9 with predominantly left tonic neck reflexes for the same period and found that 4 became left-handed and 5 right-handed. He is careful to draw no conclusions but merely comments that, although the tonic neck reflex is usually indicative of later handedness, there are interesting and significant exceptions.

He states that the strength and persistence with which the tonic-neck-reflex position is held varies greatly in different infants. It would be interesting to know if the 5 infants with left tonic neck reflexes who grew up to be right-handed were relatively weak in their tonic neck reflexes. Whether they were or not, and it seems likely that they were, it appears very probable that the 5 who changed from a predominantly left tonic neck reflex in early infancy to right-handedness in later childhood did so in response to environmental pressure. It is not wholly clear why the remaining four did not change also. It may be that their preference was unusually strong, or it may be that they were influenced by some of the secondary factors mentioned above.

Discussion

Obviously, an answer to the question whether or not it is safe and wise to train an apparently left-handed child to write with his right hand cannot be unequivocal.

It has been pointed out that there are two entirely different kinds of handedness in early childhood: one is physiologic, native, inherent, inherited; and the other is psychologic, acquired, environmental, cultural. The first is the tendency — strong in some, weak in others — to prefer to use for more difficult manipulations a particular hand, which may be either the right or the left. Apparently, from a number of reports, this tendency is never absolute, but instead shifts normally from side to side throughout infancy and the early years of childhood, often with only a relatively slight and decidedly temporary preference for one or the other hand. In most infants, however, and for most of the time, Gesell reports that the right hand is more frequently used.

The second kind of handedness, in contemporary civilization at least, is the product of a steady, rather strong, social and cultural pressure favoring the use of the right side. There is no satisfactory explanation of why in the present day the right hand is always "right." One must accept that as a fact, although there are some indications that, in other times and civilizations, the left was the preferred side.[9]

In the older child and in the adult the eventual and permanent handedness appears to be the outcome of the merging of these two influences. Environmental pressure toward the right merely strengthens and confirms native right-handedness. When the inherent tendency is toward the left it comes into direct conflict with the environmental right. The result then seems to depend upon the relative strengths of the two opposing tendencies. When the inherent left preference is strong it is able to resist more or less completely the external pressure toward the right. This situation probably accounts for the majority of left-handed persons and for those who are left-handed with some right-handed skills. When the inherent left tendency is weak, it is largely or entirely overcome by the external right, producing persons who are either wholly right-handed or right-handed with some left-handed ability.

The groups of right-with-some-left and left-with-some-right are usually classed as ambidextrous. This is an ambiguous term with no very satisfactory definition. It is generally agreed that there is no

such condition as complete or absolute ambidexterity, in the sense that both hands are equally capable in all activities. All ambidextrous persons are right-handed in shaking hands, most are in eating, and some even are in writing. What is really claimed for them is that they choose the right hand for some activities and the left for others; or else that, although apparently right-handed or left-handed, they can perform most tasks better with the nonpreferred hand than the average person can. Consequently, except for the fact that the term is firmly imbedded in the language, it would be better to abandon entirely the classification of "ambidextrous" and replace it with such terms as right-with-some-left and left-with-some-right, which come much nearer describing the actual conditions.

It should by now be clear that the safety and wisdom of teaching an apparently left-handed child to use his right hand for writing depends upon the strength of his inherent preference for the left. If this preference is strong, or if for one reason or another he has become accustomed to use his left hand for all skilled acts, to force him to wield a pencil with his right may be difficult or even impossible. Conversely, if he is already using his right hand for some activities, he may probably be taught to write with it without difficulty.

It is only rarely that the question arises of shifting an older child from right-handed to left-handed writing. It should never even be considered unless he is strongly left in other activities, is having difficulty in expressing himself orally or on paper and is wholeheartedly ready and willing to try the experiment. A number of cases have been reported in which the shift was made with beneficial results, but they certainly are not common and the change should never be advised without considerable thought.

The chances of producing stuttering by teaching an apparently left-handed child to use pencil and pen with his right hand have probably been exaggerated. When stuttering does develop under these circumstances it is as likely to indicate an inherent weakness of the speech mechanism that causes it to break down under any added strain as it is to mean that the speech center has been partly shifted to the originally nondominant side of the cerebral cortex. The latter hypothesis is an attractive one, but it has never been satisfactorily proved. The experience of many primary schools has shown that in most cases apparent left-handers learn to use the right hand for writing without suffering any disturbance of speech.[9]

Conclusions

Many apparently left-handed primary grade children may be successfully taught to write with the right hand. When writing begins they should all be so taught, because the use of the right hand fits in better with the left-to-right direction of writing and also because it conforms to the custom of the majority and hence is easier psychologically. If, however, a child objects strenuously or develops signs of nervous strain, of which stuttering may be one, the attempt should be abandoned at once, and he should be allowed to use his left hand without criticism.

Those who are taught to write with the left hand should be shown the proper position of the paper, which is slanted with the top border to the right instead of to the left as is usual. It is often necessary to drill them in the use of this position, since otherwise they are likely to imitate their right-handed neighbors. They should also be allowed to write with a slight backhand slant if they so prefer.

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EPIDERMOID CARCINOMA PRIMARY IN BARTHOLIN'S GLAND

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CARCINOMA of Bartholin's gland is one of the rarest malignant lesions occurring in the female genital tract, approximately 75 cases having been reported in the literature. In 1939, Simendinger,[1] with a detailed résumé of 38 cases, enumerated and classified the cases since Klob's[2] initial reference to the lesion in 1864. Isolated reports have subsequently appeared in the surgical literature,[3] and Boughton,[4] in a scholarly review of the problem in 1943, adjudged that by that time 75 cases had been listed, but that "a great number of these are published with inadequate data and may not be accepted as proved cases of Bartholin's gland carcinoma." Throughout such studies as have been cited and in more recent case reports,[5, 6] there has occurred a major preponderance of adenocarcinomas as compared to epidermoid neoplasms. Furthermore, in Taussig's[7] series of 155 cases of vulval cancer, only 9 originated in the vulvovaginal gland; similarly, in the files of the Worcester City Hospital, there are records of only 2 vulval neoplasms and 1 of the vestibular gland. Because of the relative infrequency and paucity of epidermoid types of tumor of this gland heretofore reported, we have been prompted to describe a case of epidermoid carcinoma primary in Bartholin's gland, which was recently treated on the wards of the East Surgical Service in the Worcester City Hospital under the supervision of one of us (J. F. C.).

INCIDENCE

The incidence of this lesion has been established between the ages of forty to fifty-five years, whereas etiologic factors have been sought in chronic irritations and infections, trauma of sexual intercourse and tertiary syphilis.[8, 11]

PATHOLOGY

Histologically, there are two types of carcinoma of Bartholin's gland: adenocarcinoma and epidermoid carcinoma. These forms are possible because the acini are lined by cuboidal cells, and the superficial ducts near the surface are lined with stratified squamous epithelium. The ducts lying between the acini and the superficial squamous-lined ducts are lined with a transitional type of epithelium, which readily undergoes metaplasia.[12-14] Honan[15] has expounded certain criteria necessary for a diagnosis of cancer primary in Bartholin's gland to be entertained. Extensive search of the literature reveals no special study of the lymphatics that drain Bartholin's gland; they are generally considered to be the same as those from the vulva, with a predilection for the inguinofemoral chains bilaterally because of the lymphatic anastomosis in the mons veneris.[4] However, no cases of bilateral involvement of these glands have been reported. Such an extension to the inguinofemoral nodes occurs with rapidity and prognosis is unfavorable, chiefly because early diagnosis is infrequent.[16] A five-year-period without recurrence is not long enough to establish cure, since recurrence may take place ten to eighteen years after operation.[17]

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SYMPTOMATOLOGY

The growth is sometimes first noted as a small, firm, nodular, painless swelling in the normal position of Bartholin's gland. At the beginning, it may be mobile, but later as the growth extends, it infiltrates the surrounding tissue and becomes fixed.[10] Enlargement of the growth is attended by pain, which is commonly referred to the coccyx and groin and is made worse by coitus and menstruation. Walking may become painful, and a fetid leukorrhea with a serosanguineous discharge from the duct of the gland may develop. As the overlying skin becomes involved in the tumor mass, the growth becomes reddened, edematous and painful to touch. With continued progression there is a tendency for the mass to become necrotic, so that the tumor may feel fluctuant and may be confused with a cyst. The neoplasm tends to grow deeper rather than more superficially and involves the surrounding fat, the muscle tissue and, later, the pubic bones.

PHYSICAL FINDINGS

Usually there is a hard, nodular swelling situated to one side of the introitus, with an intact, overlying skin surface. The labium majus pudendi may be increased in size, especially in its posterior part. The tumor is felt in the portion of the labium corresponding to the normal site of the vulvovaginal gland, and it is usually lobulated on palpation. The mass is mobile and painless on pressure, and the suprajacent skin is normally free of the growth. There may or may not be inguinal adenopathy. Diagnosis is established by consideration of the possibility of carcinoma, failure of response to conservative measures and biopsy.

TREATMENT

Proper therapy of this disease appears to be a combination of irradiation and surgery,[18] although

clinicians are not unanimous in opinion and no one surgeon's experience has been wide enough to outline a definitive course of treatment. Some advocate radical vulvectomy, including excision of the labia minora and clitoris by electrocoagulation supplemented by the extirpative inguinofemoral-lymph-node dissection of Basset bilaterally. Taussig[19] recommends that this procedure be done in two stages: excision of the vulva, followed in two weeks by the groin dissections. Others reverse this order, employing the gland dissections first, always including removal of the so-called gland of Cloquet lying within the femoral ring in juxtaposition to the femoral vessels. Still others insist on preoperative and postoperative irradiation as a vital part of the treatment. Te Linde[18] states that, in his opinion, irradiation should follow the radical operative procedures to give the patient every chance for recovery from a disease in which the prognosis, regardless of treatment, is poor.

Case Report

L. H. (W. C. H. 371197), a 37-year-old divorced woman, was admitted to the hospital on April 16, 1948, with the complaint of "a small lump" on the right labium majus pudendi of about 5 years' duration. For the last year, the mass had been increasing in size and had of late been painful enough to cause her to seek medical advice in the outpatient department. Thence, she had been referred to the hospital with a presumptive diagnosis of "chronic Bartholin's cyst on the right." History elicited by the admitting house officer revealed that the tumor had been increasing in size of late, on two occasions had discharged bloody fluid and at times had caused pain in walking. There was no radiation of the pain, and the only other time the growth caused distress was if she inadvertently compressed it at toilet.

A review of the systems was noncontributory.

The menarche had begun at 11 years of age; the periods were irregular and of 7 days' duration without clots. Pain was marked for the first day. There was no intermenstrual discharge; since an oophorectomy in 1938, the periods had occurred but once or twice yearly.

Physical examination revealed an obese woman with a pronounced alcoholic odor to the breath lying quietly in bed in no acute distress. There was a generalized psoriasis over the body. Physical findings of note were limited to the local examination: a firm, indurated, tender mass the size of a grape, situated to the side of the posterior fourchette in the position normally occupied by Bartholin's gland. No discharge could be expressed from the gland through its duct. The mass was tender, causing exquisite pain on palpation, and was reddish purple, with whitish areas shining through from deeper within the mass. It was nonfluctuant and mobile, although the overlying skin was firmly adherent. There was no demonstrable inguinal lymphadenopathy.

The temperature was 98.6°F., the pulse 88, and the respirations 20. The blood pressure was 136/82.

Examination of the blood disclosed a hemoglobin of 91 per cent and a white-cell count of 4800, with 66 per cent neutrophils, 4 per cent eosinophils, 1 per cent basophils, 26 per cent lymphocytes and 3 per cent monocytes. Blood Hinton and Kahn tests were negative. A chest film was unremarkable. The fasting blood sugar was 87 mg., and the nonprotein nitrogen 31 mg. per 100 cc.

At operation on April 21 under nitrous oxide, oxygen and ether anesthesia a pelvic examination, precluded because of tenderness of the mass on admission, was performed without remarkable note. An elliptical incision was described about 0.6 cm. around the cystic mass, which was then grasped with an Allis clamp and elevated. The mass was excised with intact overlying skin and a considerable amount of subjacent areolar tissue. It was not possible to identify the duct to the gland.

The pathological diagnosis was epidermoid carcinoma (Grade II), primary in Bartholin's gland. The overlying skin was reported as normal and intact. The patient was seen in consultation by members of the Radiology Department, who believed that at this stage surgery should be relied upon solely to grant the patient a cure. A roentgenogram of the pelvis and pubic rami showed no evidence of metastatic involvement.

On April 30, under spinal anesthesia, the labia majora, mons veneris, clitoris and labia minora were excised generously with the cutting current of the electrosurgical knife. Hemostasis was secured with electrocoagulation and No. 4 to 0 catgut ligatures where needed. The skin was then sutured directly to the vaginal mucosa, and superiorly over the pubic arch, skin was sutured directly to skin in a vertical manner, although it was under some tension. An inlying Foley catheter was introduced to compensate for urethral edema and consequent urinary obstruction. Recovery was uneventful, the catheter being removed in 5 days with ensuing normal vesical function.

The pathological diagnoses were specimens consisting of labia majora, labia minora and clitoris and acute inflammation of recent incisional site.

At operation on May 14 under spinal anesthesia, a right-sided Basset operation was performed, with opening of the inguinal canal, removal of the round ligament, division of the inferior epigastric vessels and dissection for iliac, inguinal and femoral lymph nodes. No Cloquet node was detected, but several were removed from the iliac vessels. After operation, the patient was placed on anticoagulant therapy as a prophylaxis against femoroiliac phlebitis, the blood prothrombin time being maintained at about 40 per cent of normal. The subsequent clinical course was without incident, and sutures were removed on the 9th postoperative day.

The specimen consisted of fascia and muscle tissue. The lymph nodes showed chronic lymphadenitis.

On May 28, under spinal anesthesia, a Basset operation was carried out on the left side as described above. Several lymph nodes were removed from the iliac chain, but again no Cloquet node detected. The patient was again placed on an anticoagulant regime for several days and convalesced without incident. The skin sutures were removed on the 7th postoperative day.

The specimen consisted of areolar tissue, fascia and muscle. The lymph nodes showed chronic lymphadenitis.

The patient was seen again in consultation by the Radiology Department, which preferred not to administer radiation but rather to follow the patient in the Tumor Clinic. Pelvic examination on the day of discharge showed an introitus readily admitting two fingers, with well healed suture lines. The patient was discharged on June 4, to be followed in the Tumor Clinic.

Summary

A case of epidermoid carcinoma primary in Bartholin's gland is reported, and the literature on the subject is reviewed.

The epidermoid types of tumor of this gland are rare.

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MEDICAL HAZARDS ASSOCIATED WITH THE FISH INDUSTRY IN MASSACHUSETTS

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BOSTON

THE fish industry in Massachusetts is quite extensive and is to be found primarily near Cape Ann, in Boston and around New Bedford. The principal fish brought to these ports include cod, haddock, mackerel, herring, redfish, pollock, whiting, sole and flounder. The fish may be processed for sale in a number of ways. They may be sold in a fresh state round, dressed or filleted; they may be frozen whole, dressed or filleted, they may be prepared for canning, and they may be salted, although this treatment is becoming obsolete.

In the processes in which fillets are obtained, the fish is first descaled by passing through an inclined rotary tumbler with holes in the periphery. The descaled fish is filleted by workers grasping the fish by the head and cutting strips of meat from either side. The fillets are washed, packaged and frozen or packed into cans, which are capped, sterilized and washed in a cleansing solution to remove oil or fragments of fish.

The offal derived from fish is usually called "gurry" and is used primarily for the preparation of fish meal for chicken and animal feed, fish oils for animal feeding and industrial uses, and glues. The "gurry" consists of all portions unsuitable for eating, such as the head, fins, tails, skins, entrails and scales. Some of these manufacturing processes involve considerable handling of the "gurry," frequently with a resulting dermatitis.

One of the most serious health hazards in the fish industry is dermatitis. This falls into several categories. Although salt is used in salting fish and is usually handled with the bare hand, unless the worker is suffering from skin abrasions, it apparently does not cause dermatitis. The alkali used in washing the sealed cans to remove oil or fragments of fish occasionally causes skin irritation. However, dermatitis actually due to the handling of the fish is mostly confined to the so-called "redfeed" dermatitis. This occurs only from June to September when mackerel are in season. The mackerel feed on minute crustaceans, one of the most common of which is "redfeed." The fish containing "redfeed" do not keep well after being caught. A few hours later the flesh of the fish opens, and after twenty-four hours the flesh is broken down to the spine. Hydrogen sulfide is rapidly evolved from such fish. The "redfeed," in addition to the digestive juice from the stomach of the mackerel, may cause a dermatitis to appear after one or two days' exposure. The skin, generally of the hands, becomes swollen and intensely red, with numerous superficial ulcerations. The areas affected are those in contact with the "redfeed" and occur chiefly along the palms and the sides of the fingers. Although the lesion is painful, it heals quickly upon application of mild soaks, such as boric acid or dilute epsom salts, followed by boric acid or zinc ointment, and avoidance of further contact with the material.

TUNA

The skin of the tuna is a thin, slimy membrane covering the scales, which can easily be scraped off and is said to contain a substance that is a primary skin irritant. It will cause dermatitis in anyone working for any length of time with ungloved hands.

REDFISH

Puncture wounds are extremely common when the workers handle redfish, which are usually filleted for quick freezing and principally sold in the Midwest. The worker grasps the fish in his left hand by the head, and with a stroke of the knife cuts off the boneless material on either side. Because of the fact that the redfish has numerous pointed bones extending back from its head, a puncture of the skin may occur if the fish is not held firmly. These puncture wounds are sometimes

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followed by lymphangitis and lymphadenitis, occasionally resulting in suppuration of the involved lymph nodes.

Erysipeloid

A skin lesion frequently seen along the Atlantic Coast is erysipeloid. It occurs primarily from contact with the "gurry" or the remains of any fish that has undergone putrefactive changes. In the handling of "gurry," abrasion, laceration or puncture of the skin is common, and erysipeloid may result. This has been demonstrated to be caused by the organism *Erysipelothrix rhusopathia*. Of the 100 cases analyzed by Klauder,[1] 88 were occupational in origin, and 17 occurred in persons handling fish.

There is always a history of injury, and usually one of puncture of the skin by a fish bone. Erysipeloid may develop within several hours to one or two days. The lesion is always on the hand and appears first at the site of puncture, where there is moderate pain followed by swelling and redness. The erythema progresses down the fingers into the web and frequently spreads along the adjoining finger. Swelling may be severe, interfering with function. Arthritic symptoms sometimes occur, and they may persist after the cutaneous lesions disappear. Lymphangitis is frequent, and many of the workers complain of pain and tenderness along the arm and forearm. Occasionally, there is a mild rise in temperature.

Weil's Disease

Another occupational disease experienced by fish cutters is Weil's disease or spirochetal jaundice.[2] The fish may become infected through the urine of infected rats. This disease is acquired through invasion of the organisms through the broken skin. After a varying period of several days or several weeks, the worker is aware of the onset of an acute illness characterized by chills, fever, headache, prostration and muscle and abdominal pain with nausea and vomiting. Inflammation of the eye frequently occurs, and jaundice with bleeding tendencies may appear after several days.

Fish Oils

Some workers develop dermatitis because they are allergic to fish oils. These cases are usually confined to those handling cooked fish in the canning departments.

Other Conditions

In addition to exposure to the previously described infections, the workers are exposed to dampness, inasmuch as the fish are wet and in many cases the tables and floors of the workroom are continually wet. Exposure to dampness may result in neuralgic and rheumatic affections and may also be a contributing factor to respiratory infections. Where quick freezing of fish occurs, there is a potential exposure to refrigerants. In most cases, ammonia is used, and although the refrigerant is kept within a closed system, there is always the possibility of breaks in the piping. Ammonia is a highly irritant gas and is usually soluble in water and body fluids. It affects the upper respiratory tract, and consequently the workers immediately seek the out-of-doors when exposed to hazardous concentrations. However, if they are trapped in the room and cannot escape, they may develop a severe pulmonary edema.

In plants handling the "gurry" for conversion to animal feed, it is usually necessary to minimize the decay of the fish. In some cases, this is done by spraying the fish with chlorinated water. In other plants reliance is placed upon ozone to prevent this decay. In either case, the workers are potentially exposed to either of these two gases, which are lung irritants and should not be allowed to exist in concentrations greater than 1 part per 1,000,000 parts of air.

Treatment

The treatment of any of the above untoward effects is similar to that of any contact dermatitis or infection with resulting lymphangitis and lymphadenitis or pulmonary irritation with resulting pulmonary edema.

Prevention

The prevention of dermatitis from fish may be accomplished by the use of rubber gloves. These gloves should have treads on the finger tips to enable the workers to handle the slippery fish, or they should be covered with cotton gloves. A small amount of chlorine added to the water to wash the gloves has proved helpful in destroying contaminant organisms.

Where Weil's disease is experienced, elimination of rats is necessary. The use of protective clothing, boots and gloves minimizes skin contact with potentially infected material.

Where refrigerant gases may be encountered, the area should be well ventilated, and gas masks approved by the United States Bureau of Mines for protection against ammonia or other particular refrigerants should be available in handy locations for emergency use if leaks develop in the refrigerating system. The use of proper drains and floor boards will minimize the exposure to dampness.

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MEDICAL PROGRESS

RUBELLA (GERMAN MEASLES) AND CONGENITAL DEFORMITIES*

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THE part played by rubella in the production of congenital deformities presents a serious problem in medical practice as well as in public health. The report by Gregg in 1941 of 78 cases of congenital cataract following maternal rubella aroused the attention of the medical profession to the dangers of this disease to the fetus in the early months of pregnancy. Since then numerous studies have been carried out confirming these original findings, as well as showing that other injuries to the fetus of equal gravity may ensue. Indeed, this virus appears to be capable of bringing about a pattern of defects in this early period of fetal life, consisting mainly of damage to the eye, ear, heart, teeth and brain, and these may occur singly or in combination. The entire subject of rubella was discussed, including its history, pathogenesis and differential diagnosis, in a progress report[1] in 1947. The purpose of this paper is to present subsequent material dealing with congenital defects and to bring the subject matter up to date.

At the outset it is well to recall that rubella is a disease entity unrelated to measles, and that one attack usually confers a lifelong immunity, although second attacks may take place. No vaccine is as yet available. Drugs and antibiotics exert no influence on the virus. The diagnosis rests on those characteristics that differentiate this malady from the other exanthems — namely, the absence of Koplik spots, the kaleidoscopic character of the rash, the presence of palpable lymph nodes behind the ears and not infrequently a pink suffusion of the whites of the eyes, in contrast to the sticky mucupurulent conjunctivitis of measles. All these features are variable, depending on the severity of the disease. The circumstantial evidence of a known exposure coupled with an incubation period of approximately eighteen days is always helpful in diagnosis. The rare complications — polyarthritis, thrombopenic purpura and encephalitis — are not considered here, because neither the severity of the disease nor its complications appear to have any bearing whatever on the incidence or severity of congenital deformities. The complications that are concerned here are those of rubella during pregnancy, and are the results of injury to the fetus in utero.

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MISCARRIAGE

The virus of rubella has been isolated from the blood in the early stages of this disease. Therefore, when a pregnant woman is attacked by rubella the virus appears to be capable either of finding its way through the placenta to the fetus or of disturbing the fetal metabolism. Thus, in one way or another, certain peculiarly susceptible tissues may suffer injury. The fetus may die promptly or linger along and die several months after the attack. Death of the fetus early in pregnancy frequently results in the spontaneous emptying of the uterus. When death of the fetus occurs in the later months of pregnancy, the uterus is not so ready to empty itself and may continue to retain the dead fetus for some time without any apparent injury to the mother. Just how often spontaneous miscarriage takes place in the course of maternal rubella is unknown. Two cases in which the attack of rubella occurred in the second month with spontaneous abortion in the third month have already been reported,[1] and to this I can add a similar one. In a fourth case, in which the attack was in the second month, the patient was delivered of a macerated fetus in the seventh month.

Swan and Tostevin[2] reported a miscarriage in the third month following rubella in the second month of pregnancy. Goar and Potts[3] described one stillbirth at seven months after an attack in the first month. Fox and Bortin[4] discussed a stillbirth at the seventh month following rubella in the first month of pregnancy. Ober, Horton and Feemster[5] reported 9 pregnancies that terminated in abortion or stillbirth in which the attacks of rubella were in the first four months of pregnancy in 7 cases. Indeed, in this survey conducted for the year 1943 in Massachusetts there were as many abortions and stillbirths uncovered as there were defective children. Swan[6] has recently reported 15 cases of stillbirth following rubella, in 13 of which the infection took place within the first four months. The sum total of these reports comprises 31 abortions or stillbirths following rubella, 27 of which occurred after an attack in the first four months of pregnancy.

I am firmly convinced that any effort to prevent miscarriage during or after an attack of maternal rubella is misdirected energy, since it is not in the best interest of the mother, to say nothing of the best interest of the fetus if it is alive. To my mind, the signs and symptoms of threatened miscarriage during or after an attack of rubella should be looked upon with favor. Consultation with and confirmation by a second physician, together with the written consent of the parents, is all that is required for legal protection in carrying out the surgical emptying of the uterus.

Severe Congenital Defects Following Rubella in Pregnancy

In the progress report mentioned above I recorded from the literature 521 major congenital defects after an attack of rubella in pregnancy, as against 52 reports of normal babies following this disease in pregnancy.

Since then the first quarterly report of the committee appointed by the National Society for the Prevention of Blindness and the American Academy of Pediatrics[7] gives the following additional data on 132 mothers who had rubella during the first trimester of pregnancy. Among these there were 18 normal babies. Seventy-six babies had congenital cataracts, 35 were completely or partially deaf, 67 had congenital heart lesions, 46 were mentally retarded, there was 1 cretin and 1 mongolian idiot, and 22 were microcephalitic. Two developed gross dental defects. To this can be added 21 gross defects reported in the literature (Table 1).

Normal Children Born of Mothers Who Contracted Rubella during Pregnancy

There have been reported 36 additional normal babies born of mothers who suffered an attack of rubella during pregnancy: 11 in the first, 17 in the second, and 8 in the last trimester. This gives a total of 656 defective infants as against 124 normal babies, a ratio of 5 to 1 (Table 2).

As pointed out in the previous progress report, this figure cannot be taken as the true ratio of grossly defective infants to normal babies of mothers who had rubella in pregnancy. The two sets of figures are obtained without relation to each other. Therefore, the ratio cannot be construed as the risk. Nor can the risk be properly calculated on the basis of reported cases, since it has been estimated that only 14 per cent of cases are reported[15] and congenital deformities are not reportable. The backward approach to this whole subject renders any mathematical calculation open to serious objection. The total score presented here merely represents a danger to the fetus when rubella occurs in the course of pregnancy — a danger that apparently is greatest in the first trimester as was clearly brought out in the first report of Swan et al.,[16] and confirmed by subsequent reports.

Table 1. *Severe Congenital Deformities among Children after Rubella in Pregnancy.*

Source	Total Cases	Eye Defects	Deafness	Heart Lesions	Microcephalus	Mental Retardation	Dental Defects
Wesselhoeft[1]	521	221	243	221	74	24	20
First Quarterly Report, National Society for the Prevention of Blindness and American Academy of Pediatrics[7]	114	76	35	67	22	46	2
Ober, Horton and Feemster[3]	5	3	1	4	1		
Sanderson[8]	1			1			
Pirrie[9]	1	1	1	1			
Friedman and Cohen[10]	1	1			1	1	
Ingalls and Davies[11]	3					3*	
Buffington[12]	2	1		1			
Bass[13]	6	6		1		5	
Wesselhoeft (1948)	2	1	1				
Totals	656	310	281	296	98	79	22

*Mongolism.

Table 2. *Normal Babies Born to Mothers Who Contracted Rubella during Pregnancy.*

Source	Month of Pregnancy									Totals
	0–1	1–2	2–3	3–4	4–5	5–6	6–7	7–8	8–9	
Wesselhoeft[1]	2	7	8	6	5	7	5	4	4	48
Ober et al.[5]	1	4	6	3	9	5	6		2	36
Totals	3	11	14	9	14	12	11	4	6	84
				First Trimester		Second Trimester		Third Trimester		
Prendergast[14]				28		35		21		
				4*						
National Society for the Prevention of Blindness and American Academy of Pediatrics[7]				11		17		8		
Totals				43		52		29		124

*First trimester only investigated.

It has been shown that congenital cataract of the central and nuclear type and certain congenital anomalies of the heart, such as interventricular septal defects, result from defective development in the first trimester.[1, 17] Mongolism follows arrested development taking place between the sixth and ninth weeks.[11] Thus, the stage of development of the fetus at which the agent is active determines the type of injury that may take place. The records of the cases of congenital defects following rubella in pregnancy when the time of the attack of rubella is given in relation to the stage of pregnancy are in agreement with this knowledge of embryology established prior to 1941 and in conformity to more recent studies with trypan blue, which does not reach the fetus.[18] An interesting feature in all this speculation is that maternal rubella just prior to conception,[1] as well as an injection of trypan blue to the mother rat prior to conception, can result in congenital deformities.[18]

Thus, the virus in maternal rubella in some manner, either directly or indirectly, shows a predilection for injuring certain tissues in the fetus according to the stage of fetal development. It is not understood just how the arrest of development in these organs is brought about although much theorizing is done on this subject. The fact that damage takes place in accordance with known embryologic expectancy offers supportive evidence that one is dealing with an agent that can produce predictable consequences. However, as in other infections there is always the unpredictable element of the resistance of the tissues in the host, which allow of great variability in the injury done — from complete escape to multiple serious injuries and even death. Thus, the predictable consequences of maternal rubella on the fetus are merely possibilities, which become more likely according to the age of the fetus at the time of the rubella attack. So far as the first four months of fetal life are concerned the information to date suggests a very real danger that maternal rubella may result in a serious congenital defect.

Therapeutic abortion is immediately challenged by two objections. The first is that insufficient data are at hand to warrant considering therapeutic abortion. The figures obtained by Fox and Bortin[4] and Ober et al.[5] purport to show that the risk of congenital deformities is much less than one gathers from other surveys and the total reported congenital deformities and normal births following rubella. As already stated, these data are obtained from records that are too imperfect to be reliable. The evidence against rubella, though largely on an empirical basis as yet, is sufficient to make one aware of a danger to the fetus in early pregnancy. This danger to the life of the fetus is not nearly as disastrous in its consequences as it is to the welfare of the family in the event of survival with gross congenital deformities.

The second objection is that therapeutic abortion, except to save the life of the mother, is not permissible by law in Massachusetts. The legal aspects of this situation were discussed at length in the previous progress report.[1] The statutes regarding abortion vary in different states, and not only has the fundamental law undergone changes whereby a later proviso permits a therapeutic abortion to save the life of the mother but also judicial opinion regarding this proviso offers a broadened interpretation to permit the emptying of the uterus beyond the danger to the mother's life. The law and medicine are subject to change in social evolution. The purpose of both is to protect and benefit mankind. Consequently, when some new development in the knowledge of medicine reveals any legal obstruction to the carrying out of a desirable preventive measure for the benefit of mankind due consideration should be given to the enactment of modifying statutes to meet the situation.

It is of the utmost importance to stress the fact that the birth of one of these grossly deformed babies is not simply a disaster to the individual child but that such a grossly deformed child tends to blight the life of the entire family. The mother has to give so much attention to this child that she becomes worn out in body and mind. As a result of this the other children in the family fail to get proper care. Furthermore, social-service follow-up studies show that the parents of such a defective child are often afraid to have any more children, even when it is explained to them that this will not happen again. They say that they just could not take on the care of another infant — even a healthy one. This attitude is expressed in various economic walks of life. In short, the arrival of a grossly defective child in a family not only brings unhappiness and sorrow but also definitely inhibits childbearing.

With all this in mind the medical profession must give attention to the danger of rubella in early pregnancy. It behooves physicians to investigate this problem with the same zeal that is being shown today in the study and control of other diseases. The fear of a crippling disease such as poliomyelitis makes it possible to arouse the interest and generosity of the public. The accumulation of evidence against rubella as a cause of gross congenital deformities is capable of arousing fear similar to that of poliomyelitis, and like poliomyelitis, the basis of this fear is not of death but of the serious crippling defects. It seems, therefore, that the medical profession must through its own initiative and with the support of public opinion take up this problem of rubella in a concerted drive under a national commission, rather than by sporadic local investigations. The results of such a national investigative organization would in the course of time evaluate the dangers of this disease in their true light with satisfactory figures. Along with this would be well conceived investigative work directed

toward the possibility of widespread immunization. Until work of this kind is carried out on a national scale physicians must face the problem as it lies before them today.

First of all, it becomes obvious that it is advisable for everyone to have rubella in childhood and thereby to acquire a relative, lifelong immunity. This proposition is all very well, but many children have mothers who have never had the disease and who are in the first months of pregnancy. Therefore, to encourage the spread of the disease in childhood may well increase the incidence of the disease among these pregnant mothers. Consequently, the only satisfactory solution will be an immunizing agent that does not carry with it the infectiousness of the disease itself. This has already been successfully accomplished in two virus diseases — namely, smallpox and yellow fever.

In the second place, pregnant mothers should avoid exposure to rubella. This is likewise beset with difficulties because rubella is infectious before the rash appears. For example, in the case of a woman in the first four months of pregnancy with a negative rubella history who has spent the afternoon with a friend who comes down the next day with a typical rubella, would gamma globulin do any good as a preventive measure? Theoretically, one might expect some benefit, but unfortunately gamma globulin is made from pooled blood very weak in antibodies to rubella in contrast to its content of measles antibodies. Ordinary gamma globulin has not proved effective in preventing rubella, mumps or chicken pox. The Massachusetts Department of Public Health urges physicians not to use gamma globulin except for diseases in which it has proved to be efficacious. In the case alluded to, the administration of 10 cc. of gamma globulin offers only a remote possibility of protection. If the pregnant mother already has rubella, it is hardly likely that any antibodies contained in the gamma globulin could be relied upon to protect the fetus. To my mind, in the light of present knowledge of gamma globulin, its use under these circumstances offers a false sense of security.

Barring the favorable event of a threatened miscarriage, which can lead to spontaneous or surgical emptying of the uterus, physicians in Massachusetts are placed in a medicolegal dilemma. The use of contraceptives for the prevention of disease is permitted by law. The idea of a second amendment to the law, which would permit a therapeutic abortion for the prevention of the birth of a diseased child, seems to deserve equal consideration in the interest of public health.

If all cases of rubella were reported — as they should be — and especially those in pregnant women with a note to that effect, the epidemiologic status of this disease would be better ascertained than at present, and the attendant risk of gross congenital deformities could then be satisfactorily determined. The anxiety caused by the evidence at hand regarding the danger of maternal rubella to the fetus demands that the medical profession report all cases of rubella with the utmost diligence and that the results of maternal rubella on the fetus be studied on a nation-wide basis.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

BENJAMIN CASTLEMAN, M.D., *Associate Editor*

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CASE 35071

PRESENTATION OF CASE

First admission. A forty-six-year-old carpenter was admitted to the hospital because of epigastric distress of eight years' duration.

The pain usually developed in the midafternoon and was promptly relieved by food or soda. On one occasion he vomited large quantities of bright blood.

Physical examination revealed a well developed man, with a blood pressure of 130 systolic, 80 diastolic. There was moderate exophthalmos and slight lidlag. The skin was slightly dry and cool. Examination of the chest and abdomen was negative. Urine, blood and stool examinations, including guaiac tests, were negative. Gastric analysis revealed 33 units of free hydrochloric acid. The serum cholesterol was 153 mg. per 100 cc. A gastrointestinal series showed a small ulcer crater on the lesser curvature of the stomach just above the angulus. Basal metabolic rates on six occasions ranged from −30 to −40 per cent. Electrocardiograms showed bradycardia and low T waves. Three weeks of medical management brought symptomatic relief but produced little change roentgenologically in the gastric ulcer. He was discharged to the Out-Patient Department on a bland diet and alkali therapy.

Second admission (five years later). In the interim the epigastric distress was well controlled, and the patient failed to return to the Out-Patient Department. He had continued the discharge medication of 0.1 gm. of desiccated thyroid and followed the diet rather faithfully. Nine months before this admission he gradually developed crampy, midepigastric pain about one hour before meals, which was not relieved by food or alkali.

Physical examination was essentially unchanged. The blood cholesterol was 417 mg. per 100 cc. Basal metabolic rates again ranged from −39 to −46 per cent, and the protein-bound iodine was 0.4 microgm. per 100 cc. Two gastrointestinal series again demonstrated the small lesser-curvature ulcer. Barium enemas and skull films were normal. He was placed on a six-meal bland diet and 0.2 gm. of thyroid daily, with considerable improvement, and was again discharged.

Third admission (one year later). He was fairly comfortable for three or four months, but then he became plagued again by his epigastric pain. Three weeks before entry he abruptly developed a tender swelling of the thoracic spine, which persisted unchanged. The only changes on physical examination were midepigastric tenderness and a tender, smooth swelling over the tips of the sixth and seventh dorsal vertebras. The urine was normal except for 4 or 5 white blood cells per high-power field in the sediment. The white-cell count was 8650; the hemoglobin was 14.5 gm. The cholesterol was 192 mg. and the esters 146 mg. per 100 cc., and the calcium and phosphorus were normal. A gastrointestinal series again demonstrated the ulcer, which was slightly smaller than before. There was osteoporosis of the spine and a compression fracture of the ninth dorsal vertebra. Examination of the lungs and intravenous pyelograms were not remarkable.

A subtotal gastrectomy, with removal of a benign ulcer, was done. The patient convalesced well until the seventh postoperative day, when he developed right-upper-quadrant pain following meals and worse at night. On the eleventh postoperative day he abruptly passed a thin, bright-red, bloody stool and another an hour later. The pain, which had been intermittent and crampy at onset, became sharp and steady. Abdominal examination was negative, as were plain films of the abdomen. The abdomen was re-explored, with entirely negative results. He again convalesced well without pain or bleeding until the seventh postoperative day, when the upper-quadrant distress returned and was again apparently closely related to food, coming on ten to twenty minutes after eating. This was associated with nausea, a sense of abdominal fullness and dyspnea. After several days this syndrome was expanded to include an urge to defecate, with passage of thin, loose stools immediately after the pain began. These symptoms became quite incapacitating, and the patient failed to eat and gain weight. A gastrointestinal series showed the stump of the stomach to fill well and empty readily, with no demonstrable lesion. A serum amylase was 60 units. The pain was only partially relieved by atropine and demerol, and he consistently refused to eat because of the pain. After almost two months in the hospital at his own request he was discharged on a six-meal bland diet, atropine and phenobarbital.

Final admission (six weeks later). His condition after discharge became increasingly poor. He practically refused to eat at all because of the epigastric distress, nausea and diarrhea, which invariably followed eating even the smallest amount of food. The pain came in waves, was accompanied

by loud gurglings and lasted about one hour. He became emaciated and developed dyspnea, dizziness, palpitations, sweating and flushing, which occurred erratically in time, lasted only a few minutes and was not necessarily associated with the other complaints. He also noted grossly bloody stools on several occasions.

Physical examination revealed a tired, weak and emaciated man. The skin was dry, inelastic and warm. The chest was clear. There were numerous extrasystoles. The abdomen was slightly distended, with moderate tenderness just to the right and below the umbilicus. Peristalsis was active with occasional high-pitched gurgles. Rectal examination showed tenderness on the right side, but no masses could be felt.

The pulse was 45, and the respirations 20. The blood pressure was 105 systolic, 55 diastolic.

The urine was cloudy, with a specific gravity of 1.018. Albumin and sugar tests were negative. The sediment was loaded with white blood cells but no red blood cells. The blood hemoglobin was 15.5 gm. The white-cell count was 6250, with 59 per cent neutrophils. The stool was light tan and guaiac negative. The amylase was 25 units, and the total protein 5.86 gm. per 100 cc., with an albumin-globulin ratio of 1.5; the nonprotein nitrogen was 24 mg. per 100 cc. The van den Bergh reaction was 0.4 mg. per 100 cc. direct and 0.7 mg. indirect. The prothrombin time was 20 seconds (normal, 16 seconds); the cephalin flocculation test was + in twenty-four and ++ in forty-eight hours. The cholesterol was 176 mg. per 100 cc. The basal metabolic rate was −40 per cent and remained at this level despite intravenous administration of thyroxin. A gastrointestinal series showed barium to enter the stump of the stomach and pass readily into the efferent loop. There was no evidence of obstruction or marginal ulceration.

Numerous diagnostic studies were instituted in attempts to elucidate further the nature of the disorder, but the patient's course was little affected by the procedures tried. The appearance time of indigo carmine was five and a half hours. A glucose tolerance test showed a fasting blood sugar of 96 mg. per 100 cc., with a rise of 137 mg. in half an hour. The levels at one, two, three, four and five hours were 126, 111, 78, 69, and 72 mg. per 100 cc., respectively. A vitamin A tolerance curve showed a fasting level of 1.3 units per cubic centimeter, and there was no rise at all in the subsequent specimens. A right splanchnic block (sixth to twelfth dorsal segments) with procaine was done, which diminished somewhat the pain during the period of anesthesia but did not relieve the tenderness. A differential spinal block was attempted, and with loss of pinprick sensations to levels of the second dorsal segment he was able to drink milk without pain, but the sense of distention and fullness was not altered. He continued to starve himself because of the severe symptoms initiated by ingestion of food, and his condition deteriorated rapidly.

An intensive program of tube and intravenous feedings was undertaken, but he tolerated the tube feedings poorly, and they were discontinued. An abdominal exploration and feeding jejunostomy was done. No abnormalities were made out at the time of exploration. Postoperatively he continued to have the same severe midepigastric pain and marked nausea and vomiting. On the fifth postoperative day he began to vomit blood, and serosanguineous material exuded from the jejunostomy wound. He developed abdominal distention and diffuse abdominal tenderness. The blood pressure dropped to 60 systolic, 40 diastolic, and there were practically no peripheral pulses. He remained in a shock-like state throughout the day despite supportive measures and died quietly late that night.

Differential Diagnosis

Dr. Arthur W. Allen: I would like to have someone tell me whether the cholesterol esters (146 mg. per 100 cc.) were within a normal range.

Dr. Chester M. Jones: That is about normal.

Dr. Allen: Thank you.

What about the vitamin A?

Dr. Perry J. Culver: It is a slightly high level. This indicates absorption and rise after a dose of vitamin A.

Dr. Allen: I would like to see the x-ray films. It is a long case and a very complicated one, and unless I can get some help here I am not going to be able to tell what was the matter with this man.

Dr. Stanley M. Wyman: I do not know how much of the original examination to show, Dr. Allen. These first two gastrointestinal examinations demonstrated in essentially the same position a crater just above the angle, which by x-ray examination appears grossly benign. As you recall, the benign character was confirmed at the time of the subtotal gastrectomy. He has a calcified aorta, which is unusual for a man of this age.

Dr. Allen: Are there any esophageal varices?

Dr. Wyman: No; but he does not have a large spleen. Without splenomegaly varices would be quite unusual.

This film demonstrates the calcified abdominal aorta a little better, which is distinctly premature for a man of this age. The film of the thoracic spine, taken because of the swelling over the sixth spinous process, shows a compression fracture of the ninth thoracic body. The bones are quite osteoporotic for a man of forty-six, and one can see the dense calcification of the aortic arch — again, an unusual finding.

The first films of the stomach and upper gastrointestinal tract taken postoperatively show the stoma to be of good width. There is diffuse thickening of the gastric folds, but I cannot identify any evidence of ulcer at the stoma or other evidence of localized disease.

DR. ALLEN: Is there active peristalsis?

DR. WYMAN: Just a little overfilling of proximal small bowel because the barium ran through to the jejunum so rapidly.

DR. ALLEN: Is this the afferent loop?

DR. WYMAN: It must be. This shows a fairly normal transport of barium at the time of the examination, the barium reaching the ileum in about three hours. The most striking thing, to my mind from these films, is the presumptive evidence of premature senility in a man of forty-six. The osteoporosis of his bones, the arteriosclerosis and his chest all make him look considerably older than the age of forty-six or even fifty. This film shows a slight increase in the anteroposterior diameter of the chest and degenerative changes in the thoracic spine with moderate osteoporosis, and the heart itself is not remarkable except that the aorta is calcified.

DR. ALLEN: This is a very complex problem, and this man was prematurely old as demonstrated by the advanced arteriosclerosis and so forth. Also there was an extraordinary persistence of a very low metabolic rate, even in spite of thyroid therapy. That is very unusual. I do not know how to explain it. At one time the pulse was recorded at 45. His story gives me the impression of a hibernating animal, with his ability to subsist on a small amount of nourishment for an unusually long period in a situation that probably would have produced a fatal outcome much more quickly in the normal person. There are many things about this that I do not understand. I am not sure what other conditions could produce such a persistently low metabolic rate. I am inclined to think that it was correctly recorded. Obviously, the examiners were quite interested in the low metabolic rate, and the protein-bound iodine was, according to Dr. Cope's information, which he was kind enough to give me, quite low and consistent with the low metabolic rate at that time.

The long duration of the ulcer symptoms is a pretty good indication that he had a benign lesion rather than a malignant one. He did very well with this ulcer, though it apparently never healed. The change in the type of pain, which had previously responded to food and alkalis, suggests that perhaps something else was developing — something that also caused epigastric distress, but no longer of a type relieved by food and alkali. It might be fair to assume that perhaps this new development was not related to the lesser-curvature ulcer.

I do not know why the skull films were done, but they bring to mind the possibility of some cerebral lesion such as that described first by Dr. Harvey Cushing[1] — the association of lesions in the midbrain with ulcerations in the duodenum and in the stomach. I do not believe that is a very likely possibility here, but it came to mind when I read this report.

The osteoporosis is interesting, and taken with the spontaneous fracture of the ninth dorsal vertebra, makes me wonder whether it was simply dietary or whether there was some basic underlying metabolic disturbance that is not clear to me. I do not know what the explanation would be. This one instance of high recording of blood cholesterol, I think, might be a typographical error. It is listed at 417 mg. per 100 cc. while every other one (and many others were done) was in a normal range.

DR. JACOB LERMAN: It was before treatment.

DR. ALLEN: That is the only time, before treatment, that we get any such level.

The operation performed, I suppose, was a subtotal gastrectomy, with doubtless removal of the distal half or two thirds of the stomach, including the ulcer on the lesser curvature. There is nothing unusual about that. It was undoubtedly assumed that the bleeding experienced previously originated from the ulcer. Then when he bled on the eleventh postoperative day the surgeons were disturbed because they wondered if it had anything to do with their suture line or whether they had overlooked some other lesion. Of course, it is possible for a man to have an ulcer in the stomach and duodenum as well, and the ulcer in the duodenum might be far enough down so that the duodenal stump can be turned in without too much awareness of the situation on the part of the surgeon.

The change in the character of the pain nine months before he came in the second time makes me believe that he did have something besides this ulcer of the lesser curvature. The fact that he bled after resection, as late as the eleventh day, makes me believe that he bled, not from the suture line, in which case bleeding should have taken place about the seventh day or earlier, but from a lesion, whatever it was, that produced a change in symptoms and may very well have been related to the final outcome. The fact that he was re-explored and nothing found wrong with the anastomotic site and no cause for the pain determined makes me wonder if this man had a lesion that could not be found within the abdomen by ordinary methods. Could he have had a hidden lesion in that portion of the duodenum that cannot be seen readily without opening the mesentery over it, or could the bleeding have come from above?

The symptoms described here suggesting the dumping syndrome are interesting, but I am not of the opinion that this man could have had such a severe course, with the outcome as it was, on the basis of a dumping syndrome alone. In some gastrectomized patients, the percentage is low, there is too rapid emptying of the stomach segment into the jejunum, with the symptoms described here — discomfort, usually called distress in the epigastrium, nausea and sweating that last for variable periods of time and usually go away about thirty minutes after the ingestion of food, particularly

if the patient lies down. The postoperative symptoms in this man were more severe than that. They were so severe that he did not dare take any food at all, because it initiated a gastrointestinal reflex, which was very marked, giving a five-and-a-half-hour time from the ingestion of carmine to the discharge of the dye from the rectum. That is a very rapid intestinal rate. Doubtless it is on that basis that the various tests were done on the parasympathetics and with spinal anesthesia.

A feature about this case that is disturbing and that I cannot understand is why this man had tenderness in the right lower quadrant. I cannot see why he should have right-lower-quadrant tenderness just on the basis of his rapid intestinal rate. It is conceivable, I suppose, that he did have a lesion in the cecum, but all the examinations with barium enema prior to operation failed to reveal any difficulty in the right colon.

The whole situation is further confused by the fact that, if I am interpreting this correctly, this man died of hemorrhage. It is very unusual to die of hemorrhage these days. There is usually enough blood around and it keeps going in and usually death can be staved off for an incredible length of time by that means. This man on his final day, being in a poor nutritional state, began to bleed and serosanguineous material came from the jejunostomy tube. He developed abdominal distention, with diffuse abdominal tenderness. It does not state whether he still had peristalsis. One might like to know that because, even in a man as sick as this, if we assume that all he did was to bleed to death, I think he still would have had peristalsis. If he had peritonitis, however, he would not have peristalsis. The fact that the man vomited blood and blood came from the jejunostomy tube probably rules out a source of hemorrhage lower than the high jejunum — that is, we must look for something from the esophagus, from the stomach, from the duodenum or from the first portion of the jejunum.

I wonder whether that is a fair deduction — whether or not he had something else. I am not prepared to say where the bleeding came from. We have these various sources of bleeding that we know about, — the esophagus, usually esophageal varices, and lesions in the stomach of all kinds, — but it is hard to believe that he could have had leiomyoma or cancer of the stomach or ulcer of the stomach that would not have been palpated at the last exploration. He could have had gastritis, I suppose. People have bled to death from gastritis alone. We have at least 2 cases in this hospital in which that has occurred. He could, I suppose, have had duodenal ulcer far down that was never felt and never demonstrated, from which he could have bled. He could have had a diverticulum of the duodenum, which was not picked up on x-ray examination and not seen at exploration. He could have had in that duodenum gastric mucosa from which he could have bled. An ulcer could also have perforated finally into the peritoneal cavity, resulting in peritonitis.

Dr. Tracy B. Mallory: There is a note that in the final three hours peristalsis was minimal and sluggish.

Dr. Allen: Still present?

Dr. Mallory: Apparently.

Dr. Allen: That would make it necessary for me to believe that this man bled to death from whatever lesions he had. I do not think we should forget the pancreas. He had had at one time slight elevation of the serum amylase. I doubt if pancreatitis would have lasted as long as this. The necrotizing type of pancreatitis causes death in the neighborhood of forty days, and erosion of the splenic vessels sometimes occurs with perforation into the colon or stomach, resulting in death by that route. It could, I suppose, have eroded into the duodenum or the jejunum, and the blood might have come from some such source. I doubt that we have enough evidence to back up erosion of the splenic vessels from pancreatitis.

Now, of course, I do not know how far general systemic disorders could have played a role in this case. It might be something that I have never heard of. At any rate, I must get through because I know a lot of you want to discuss it. This man had a gastric ulcer. We assume that he had hypothyroidism and marked arteriosclerosis, and he had a compression fracture of the ninth dorsal vertebra on the basis of osteoporosis and extreme malnutrition. Of all the things I can think of that satisfy me as to the final cause of death and the source of all his bleeding a lesion in the third portion of the duodenum, which I am going to assume was probably a diverticulum, is the most probable.

Dr. Mallory: This patient puzzled everyone in the hospital as much as he has Dr. Allen. Almost everyone saw him and made a note at one time or other.

Dr. Cope, have you anything to say?

Dr. Oliver Cope: No one thought of Dr. Allen's diagnosis. We should have considered it; practically everything else was considered. The Pathology Department did one kindness to Dr. Allen. They left out some of the data that attracted attention way out in left field. In addition to hypothyroidism, the question was brought up as to whether he might have hyperparathyroidism. Dr. Allen referred wisely to metabolic disturbances that might have given rise to the ulcer. We debated this back and forth, for there was a suggestion that he had hyperparathyroidism and coincidental ulceration in the upper intestinal tract. It was a good thought, but no one could make the diagnosis.

No one could understand why he had the pain, and I think it was fair to summarize the clinical opinions as follows: there was a suggestion of hyper-

parathyroidism, which was excluded because the evidence (I will not go into the data in detail) was equivocal, perhaps because the patient did not respond to thyroid. Dr. Lerman will talk about the response to thyroid in a moment.

The neurosurgeons could not explain why he had pain. They thought that the only way to prevent pain was to go to the highest center — in other words, to do a lobotomy. The lobotomy would also have helped in the management, for the patient was suspicious and extremely difficult to handle. The Medical Service did an extraordinary job in keeping him alive. He required an enormous amount of care for four months throughout which he was in an extreme state of malnutrition. Finally, another point of view, which was the point of view adopted, was to re-explore the abdomen as a final measure on a chance that some lesion had been overlooked — the type of lesion Dr. Allen referred to. Such an exploration was recognized to carry a high risk in a patient in such a condition and particularly since no one had any firm idea of what might be wrong. Exploration was carried out by Dr. Welch.

Dr. Lerman: I think there is no doubt about the diagnosis of myxedema. On the first admission the diagnosis was suggestive. When he came back the second time it was very obvious. Of theoretical interest is the possible etiology. He did have signs of residual exophthalmic goiter. The question arose whether it could be a rare type of hyperthyroidism that had burned out, with resulting myxedema. He responded to a special preparation, which we were using, called tetrabromthyronine. The statement is made that he did not respond to thyroxin. That is not true. The response was poor, but he did respond at one time to a dose of 1 mg. of thyroxin for ten days when the basal metabolic rate went from −40 to −25 per cent, which is a poor result. The explanation for the response was that he was in such a poor nutritional state that he could not get up enough steam to make a response. It is interesting to speculate on the relation between prolonged myxedema and arteriosclerosis. It seems reasonable to expect that the hypercholesterolemia of myxedema will lead to extensive atherosclerosis in large and small vessels.

Dr. Jones: When I saw him several times at the request of the surgeons, it seemed to me justifiable to explore again, even in the absence of any positive findings, because of the intensity of the pain. It was directly connected with food. It was repeated over and over again; I am sure it was not a dumping syndrome. The pain was too severe for that. The main thing was that he did have a real intra-abdominal disease. We did not think he had an ulcer, as a matter of fact — at least, I thought he did not. I thought it was possible that he had a kinking with some obstruction by which pain was produced by peristalsis from time to time after intake of food, and we decided that the only way to help was to go in and explore again, trying to find a lesion that might be treated.

Dr. Claude E. Welch: His outstanding symptom was pain. We thought that cancer of the pancreas would be the most likely diagnosis, but we really expected to find nothing. We found nothing.

Dr. Allen: I would like to add one thing. I did not mention the possibility of an anastomotic ulcer because of final bleeding. It is extremely unusual if it ever occurs following a gastrectomy for a gastric ulcer.

Clinical Diagnoses

Abdominal pain of unknown etiology.
Myxedema.
Arteriosclerosis.

Dr. Allen's Diagnoses

Gastric ulcer, postoperative.
Osteoporosis, with compression fracture of ninth dorsal vertebra.
Arteriosclerosis.
Hypothyroidism.
Duodenal diverticulum.

Anatomical Diagnoses

Atrophy of thyroid gland, with myxedema.
Arteriosclerosis, severe, of aorta and mesenteric vessels.
Congenital anomaly of mesenteric arteries, hypoplasia of celiac axis and hypertrophy of superior mesenteric.
Thrombotic occlusion, old, of celiac axis.
Thrombotic occlusion, fresh, of superior mesenteric artery.
Incipient gangrene of small intestine.
Osteoporosis.
Slight hyperplasia of parathyroid glands.

Pathological Discussion

Dr. Mallory: At autopsy in this case, the lesion found was in the mesenteric vessels. He had what I am quite sure was an anomaly to start with. The celiac axis was very small, and the superior mesenteric artery very large. The inferior mesenteric was also small, but I would assume the celiac axis was half normal diameter and the superior mesenteric was twice normal diameter. The celiac axis was almost completely occluded by an old, organized thrombus, and a large anastomotic vessel was found connecting the superior mesenteric and pancreaticoduodenal arteries. The stomach and spleen must have been nourished from the superior mesenteric artery through various anastomoses. The terminal episode was an acute thrombosis of the superior mesenteric, which had cut off the blood supply of almost the entire intestinal tract between

the esophagus and the colon. It was partially infarcted. At autopsy we found no intrinsic lesion in the remainder of the stomach or elsewhere in the intestinal tract. So I think the sclerotic changes in the mesenteric vessels probably were the cause of the persistent pain. At least, we have no other explanation for it.

A few other findings at autopsy were interesting. The thyroid gland was almost completely atrophic, and in numerous sections we were able to find only four or five recognizable thyroid acini. The rest was reduced to fibrous tissue. The parathyroid glands seemed slightly hyperplastic. Certainly, the proportion of parenchyma to fat cells was increased, but because of the emaciation the ratio may have been disturbed by loss of fat cells. The pituitary body was normal.

DR. JONES: This could be explained, it seems to me, on the theory that the patient had a minimal local blood supply, and the minute one increased the demand for blood by putting in food, the local blood supply was inadequate and it caused "anginal" pain.

DR. MALLORY: The abdominal aorta was extraordinarily sclerotic, as shown in the x-ray films, and the atheromatous plaques markedly narrowed the mouths of all these arteries. There was also sclerotic involvement of the vessels themselves.

DR. COPE: May I ask Dr. Allen to comment finally? Our impression, in retrospect, is that the patient had abdominal angina. I have never seen this before. Is that a reasonable diagnosis to entertain here?

DR. ALLEN: I think it is. I think that is all right. It has been reported. Cushman and Kilgore,[2] of San Francisco, reported a case. Dr. Jones's explanation is quite reasonable. I think a man who has angina pectoris gets an attack with an increased demand on the heart. Therefore, it seems to be a very reasonable deduction that increased demand on the stomach caused this epigastric pain. But it is a little hard for me to understand why he bled so much from the stomach — a little difficult for me to understand why, in other words, an organ that had insufficient blood supply should not be less likely to bleed than the normal.

DR. COPE: He bled after both operations.

DR. ALLEN: And before.

DR. MALLORY: I think it is important that the coronary vessels were in good shape. There were a few thrombosed plaques, but no significant narrowing. The possibility of cardiac angina with reference of pain to the abdomen is therefore improbable.

DR. COPE: In summary, you think it is reasonable to make a diagnosis of prolonged myxedema and atherosclerosis with abdominal angina?

DR. MALLORY: That is the best explanation I can give.

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CASE 35072

PRESENTATION OF CASE

A nineteen-year-old girl was admitted to the hospital because of severe headache and right orbital swelling.

She had been perfectly well until five days before admission, when she began to have intermittent pain behind both eyes and over the right side of the face and head. The pain became progressively more severe and three days before entry was constant and prevented sleep. At this time tearing of the right eye and dripping of a clear fluid from the right nostril developed. On the following day she developed photophobia in the right eye and vomited three times. Twenty-four hours before admission a short trial with ergotamine tartrate was unsuccessful, but it was thought that she improved following pyribenzamine. There was no fever. However, the pain increased, and that night the right eye began to swell.

Physical examination revealed a well developed and nourished girl who was very drowsy but capable of being aroused and of performing simple tests. The skin was hot. There was marked swelling about both eyes with chemosis, moderate proptosis and supraorbital tenderness, more pronounced on the right side. There was thought to be slight peripapillary edema of the retina. The pupils measured 3 mm. in diameter and reacted briskly to light. The external movements of both eyes were "reduced in all directions." There was marked tenderness on the right side, and slight tenderness on the left in the preauricular region and over the right lower jaw. There was a small amount of purulent secretion (less than 1 cc.) in each nostril. The middle and inferior turbinates were slightly injected bilaterally. The ears were normal. The neck was rigid, and Kernig's sign was positive. There was dullness over both lung bases posteriorly; breath sounds over the left base were coarse and high pitched on the right. There was tenderness in both upper quadrants of the abdomen and costovertebral-angle regions.

The temperature was 103°F., the pulse 80, and the respirations 32.

The urine was normal. The blood hemoglobin was 11.5 gm.; the white-cell count was 16,500, with 86 per cent neutrophils. A blood culture was later reported to have grown *Staphylococcus aureus*. A lumbar puncture revealed cloudy spinal fluid under a pressure equivalent to 270 mm. of water. Jugular compression on the right produced no change in pressure; on the left it resulted in a good rise. The

cell count was 7000, with 93 per cent neutrophils. A culture was negative.

The patient became more stuporous, and the temperature rose to 104°F. Roentgenograms of the skull and sinuses were normal. She was immediately started on penicillin, streptomycin and intravenous heparin. On the second hospital day the temperature was still elevated; the prothrombin time was 25 seconds (normal, 16 seconds), following which dicumarol therapy was begun. It was noted that the left eye had become as swollen as the right. A second lumbar puncture produced a cloudy, yellow-tinged spinal fluid containing only 481 white cells per cubic millimeter. On the fourth hospital day the prothrombin time was in the neighborhood of 50 seconds (normal, 18 seconds). On the same day the patient had a seizure consisting of clonic movements of the left side of the body, beginning in the face and extending downward, lasting about a minute. Several more seizures occurred but ceased after she had been given dilantin and phenobarbital. Later that day she was semicomatose and found to have a left hemiparesis and hemianopsia. The white-cell count had fallen to 4700, with 80 per cent neutrophils; sulfadiazine administration was stopped. On the next day, however, these last findings had cleared considerably, and although the temperature still fluctuated between 101° and 102°F., she seemed much improved. There had been a progressive reduction in the number of cells in the spinal fluid. The periorbital swelling was considerably reduced, and she was able to open her eyes and look around. On the eighth hospital day, after continued improvement, she complained of chest pain, first on the left and later on the right, accentuated by deep inspiration.

On the following day the white-cell count had risen to 12,300. There was no cough or hemoptysis, and examination of the legs was negative. A roentgenogram of the chest disclosed three small areas of increased density overlying the posterolateral portions of the fifth and seventh ribs on the right side and the ninth rib on the left. Heparin was again started. Twenty-four hours later she appeared acutely ill, pale and moaning. The temperature was 101°F., the pulse 90, and the respirations 25. There were tenderness over the right temple, and tenderness, marked redness and edema of the right eyelid. The right eye was proptosed, and the conjunctiva showed severe chemosis with slight, pink tearing. There was moderate nuchal rigidity, and a positive Kernig's sign, more marked on the left. A lumbar puncture revealed a spinal-fluid pressure equivalent to 180 mm. of water and containing 28 neutrophils per cubic millimeter and a negative smear and culture. On the following day the fundi showed retinal edema, the disk margins were blurred and indistinct, and there was a suggestion of papilledema. The prothrombin time was 24 seconds (normal, 16 seconds).

After another brief period of improvement the patient began to complain of severe pain in the eyes and right ear. She was drowsy most of the time. On the next day she complained of the pain almost constantly and was obviously much weaker. Later in the same day she tried to vomit but could only retch, shortly after which she became unresponsive. The left corneal reflex was absent. There was ankle clonus, moderate on the right and slight on the left, and a positive Babinski on the right. She remained unresponsive and died several hours later, on the thirteenth hospital day.

Differential Diagnosis

Dr. Augustus S. Rose: From the history, physical findings and course of this patient we have little question regarding diagnosis. It is obvious that the patient had an infectious process involving the dural sinuses, and in view of the positive blood culture for *Staph. aureus* and the early response to therapy we must assume that the infecting organism was *Staph. aureus*. There are a number of questions, somewhat unanswered, that require consideration. In the first place, we are told that she was well until five days before admission, eighteen days before death. This is a very rapid termination, particularly in view of the excellent therapy on admission to the hospital, which included sulfadiazine, streptomycin and penicillin. If *Staph. aureus* was the only organism, these therapeutic agents should have done — or we would have hoped that they would have done — a better job in arresting the infectious process. The question that bothers me most of all is the source of the infection. The patient was apparently entirely well, no mention being made of a pimple or other local infection on the face or within the nose. The only leads we have are the early symptoms and the finding of pus in the nose. Back in the days before chemotherapy the development of cavernous-sinus thrombosis, which I believe this patient had, was sufficient evidence for immediate consideration of ethmoid sinusitis in the absence of infection on the face. Despite a negative x-ray examination, an acute infection of the ethmoid sinuses may have been the original source of infection. The first symptom recorded was pain behind both eyes, followed very quickly by pain in the face, on one side, and some tenderness and then swelling. Presumably because of the absence of fever, her physician thought of migraine, for which he prescribed ergotamine, and also of a histamine reaction of some sort because of the pyribenzamine. With the entire case before us, the pain behind the eyes makes me think of ethmoiditis. But probably at this time the patient had already begun to develop thrombosis of the cavernous sinus, chiefly on the right. The thrombus was probably infected from the beginning despite the absence of fever. With rapid succession there was swelling of the right eye,

followed in a day by swelling about the other eye. The thrombosis or thrombophlebitis of the cavernous sinus on the right spread via the circular sinus to involve the cavernous sinus on the left. We then have the information of a lumbar puncture done on admission, which showed no rise in spinal-fluid pressure on compression of the right jugular vein, giving evidence that the right lateral sinus had become occluded by the thromboinfectious process. The patient was drowsy, showing considerable involvement and disturbance in function of the brain, and the spinal-fluid pressure was elevated, indicating that venous return from the brain was interfered with. The cell count in the spinal fluid of 7000, predominantly polymorphonuclears, does not of necessity mean a bacterial infection of the surface of the subarachnoid space. But it does point to infection nearby. The two negative cultures of spinal fluid and the absence of bacteria support the concept.

The patient complained of pain in the chest. The House Service evidently thought in terms of emboli because they give us a negative report on the veins of lower extremities, and we also are told that she did not have hemoptysis. X-ray examination, however, showed a shadow in the lung consistent with pulmonary embolus, and I expect that it was an infected embolus without abscess formation. Eighteen days following the onset of the illness is too short for an abscess to form in the lung or in the brain.

The patient was drowsy and had a convulsive seizure on the left side, the opposite side from the occlusion of the lateral sinus. I would reason that the thromboinfective process had extended backward through the sinuses of the dura into the veins of the brain itself and had caused changes within the brain, which may well have been the beginning of an abscess. If she had survived, it is possible that she might have had a circumscribed abscess within the brain, but I doubt if autopsy revealed definite abscess formation.

One other question is, Why did not adequate treatment, which she presumably had, stop the infection? I have to leave that unanswered but assume that this patient's resistance was low, that the virulence of the organism was great and that, by the time treatment was started, infection had already spread not only into the blood stream and cavernous sinuses but also beyond and was an overwhelming infection.

I then summarize by saying that I believe the patient had a primary infection in the ethmoid sinuses from which there developed a thrombophlebitis involving the right cavernous sinus, the right lateral sinus, the left cavernous sinus, the veins of the brain, septicemia, pulmonary infarct and possibly a beginning abscess on the right side of the brain.

Dr. Tracy B. Mallory: Are there any interesting x-ray films?

Dr. Stanley M. Wyman: I doubt if they are contributory.

Dr. Mallory: Are there any questions or comments?

Dr. James B. Ayer: The test for lateral-sinus thrombosis on the right is more accurate than that on the left, so I think Dr. Rose's reasoning is probably correct.

Clinical Diagnoses

Cavernous-sinus thrombosis.
Meningitis.
Sinusitis.
Pulmonary emboli.

Dr. Rose's Diagnoses

Ethmoiditis.
Thrombophlebitis, cavernous sinuses and right lateral sinus.
Thrombophlebitis of cerebral veins, with cerebral necrosis.
Septicemia.
Pulmonary emboli.

Anatomical Diagnoses

Ethmoiditis and sphenoiditis.
Thrombophlebitis of cavernous sinuses and tributary cerebral veins.
Venous cerebral infarction.
Massive cerebral hemorrhage.
Subdural hemorrhage.
Meningitis, healed.

Pathological Discussion

Dr. Charles S. Kubik: The posterior ethmoid cells and sphenoid sinus contained not thick pus but brownish-orange, thick fluid. That presumably was the source of infection along veins of the air sinuses, which empty into the cavernous sinuses. The venous sinuses, with the exception of the cavernous sinuses, were normal. The cavernous sinuses were removed intact with the central portion of the sphenoid bone, sphenoid sinus and posterior ethmoid cells, and on microscopical sections were found to contain purulent exudate and organized thrombi on both sides. There was also infection in the circular sinus, which passes around the pituitary gland and connects the two cavernous sinuses. It is through the circular sinus that infection extends from one side to the other. In the right posterior parietal and temporal regions there was a subdural clot of blood, 0.2 or 0.3 cm. in thickness and 3 to 4 cm. in diameter. There was blood, apparently fresh, in the subarachnoid space, extending medially to the base of the brain, and a large cerebral hemorrhage, measuring between 4 and 5 cm. in diameter, in the right posterior parietal region.

On microscopical examination there was a fair amount of organization of the subdural hemorrhage, indicating that it must have occurred at least a number of days before death. The cerebral and subarachnoid hemorrhage appeared to be recent. In the same region there were thrombosis of cerebral veins that drained into the cavernous sinus and hemorrhagic foci of necrosis of the brain such as occur with arterial and sometimes with venous occlusion. I believe that thrombosis unquestionably extended in retrograde direction from the cavernous sinus to tributary cerebral veins, as suggested by Dr. Rose, and resulted in venous infarction of the brain. Infarcts of the brain, following arterial occlusion, usually are pale with hemorrhagic areas here and there, resulting from innumerable, small, diffuse extravasations and capillary hemorrhages. Venous infarcts are much more likely to be hemorrhagic. Massive hemorrhages are unusual. In this case I believe that the terminal event was a massive hemorrhage, which began as the usual type of hemorrhagic venous infarction. Microscopical examination indicates, I believe, how the large hemorrhage developed. There were some foci of infarction with a few, punctate hemorrhages and other similar foci, with a small, massive hemorrhage in the center. It seems likely that the large hemorrhage began in the same way, or possibly as a number of such small lesions.

There was no grossly visible pus in the orbital tissues — only some punctate, hemorrhagic foci. Microscopical examination of the orbital tissues revealed the ophthalmic veins filled with bland thrombi and surrounded by partly organized hemorrhages and, on the right side, a small, partly walled-off abscess. The optic and oculomotor nerves looked normal.

The spinal subarachnoid spaces contained a few lymphocytes, plasma cells and large mononuclear cells, and there was possibly slight arachnoid fibrosis — actually surprisingly little reaction, even for recently healed meningitis. The spinal cord itself and the spinal nerves were normal.

There had been indications of considerable clinical improvement for a time after treatment was begun. The mental status improved, proptosis diminished, ocular movements returned, and cells in the spinal fluid dropped from 7000 to 28 per cubic millimeter. The pathological findings also suggest that the natural course of the disease had been greatly modified. Before sulfonamides and antibiotics were available, thrombophlebitis of the cavernous sinus was invariably fatal, at least when it occurred in the severe form observed in this case. At post-mortem examination the cavernous sinuses were distended with pus, and the orbital tissues were honey-combed with abscesses. In this case it is quite possible that recovery would have taken place but for the hemorrhage.

Dr. Rose: Do you believe that the heparin and dicumarol aided the process of intercerebral bleeding?

Dr. Kubik: I think that is quite possible. We have suspected it in cases of subacute bacterial endocarditis, treated with anticoagulants, in which massive cerebral hemorrhage of the brain occurred, apparently in a region of embolic infarction.

Dr. John B. Stanbury: Were there any thrombi in the vessels of the neck?

Dr. Mallory: None were found outside the cranial cavity. In the lungs there were multiple, irregular areas of hemorrhage having the appearance of very fresh, slightly atypical infarcts some of which showed beginning softening in their centers, suggesting that they were septic in character, not as yet broken down into frank abscesses. They were too recent for that.

A Physician: How much penicillin was she given?

Dr. W. H. Timberlake: She received amounts varying from 100,000 to 500,000 units every three hours.

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EX LIBRIS

Two of the important factors that distinguish man from less elevated animals are the ability to reason and the capacity for speech. A refinement that has enabled each generation of mankind to profit most fully from the experiences of its predecessors has been the recording of ideas and the preservation of these records, whether carved in stone or scratched in tablets of clay; whether traced on papyrus or written in manuscripts or impressed upon the printed page.

Only by consulting its records has man been able to build adequately upon the experiences of the past; of greater importance to his progress than the invention of the wheel has been his establishment of the library, which contributes to his cultural and spiritual as well as to his technical advance.

Some of the brightest chapters in the story of mankind have been illuminated by the development and preservation of literature. Some of the darkest pages in history have been punctuated by the destruction of libraries and the burning of books, from the conflagration at ancient Alexandria to more recent attempts at the destruction of modern culture.

The library as an institution has been one of man's sacred heritages. This applied to the first Sumerian tablet that was laid aside to tell its story four thousand years later; it applies to the most recent text that has been placed on file. This institution is an urgent public charge, from the Library of Congress, supported by an assessment on all the taxpayers, to the smallest village library in existence. And not the least important of these repositories of learning is the Boston Medical Library, which has happily become, as emphasized recently in these pages,* one of the solemn responsibilities of the Massachusetts Medical Society.

In making his contribution to the perpetuation of a library and the continuance of its services, the responsible citizen, whether layman or physician, by no means has in mind what particular benefit he as an individual will derive from it. He can no more calculate the returns on his investment in terms of personal advantage than he can the returns from his contributions to a hospital, the Red Cross, the Salvation Army, the community chest or his church.

The Massachusetts Medical Society has voted an increase in its annual assessment to $25. Of this sum, $5.00 from each fellow was allocated to the use of the Boston Medical Library, and has proved to be a most welcome transfusion for this invaluable institution. The discharge of this barest obligation, however, is not enough. There must be in addition an increasing number of thoughtful and responsible physicians willing and eager to pay an additional $15.00 for fellowship in the Library — not for themselves but to help in preserving the very foundations of their profession.

Nor is this enough. The immediate future of the Library requires the expenditure of $75,000 for the erection of new stacks, an expansion that is neces-

*Editorial. Budget for 1949. *New Eng. J. Med.* 239:155, 1949.

sary in order that the institution may continue to rank among the foremost medical libraries of the world. This cannot be done from current income, even if augmented by the accession of new fellows. It must be accomplished as the result of an intellectual renaissance among the physicians of New England, expressed in terms of a material contribution that some modern form of alchemy can convert into the metal of which such equipment is constructed.

MEETING OF THE COUNCIL

THE midwinter meeting of the Council of the Massachusetts Medical Society, held on February 2, would have been of particular significance because of one fact alone. That was the unanimous approval of the action of the Executive Committee in authorizing the Secretary to proceed, as an agent of the American Medical Association, in collecting the assessment that the Association has levied on its members.

Of further significance was the Secretary's report that within two weeks of the mailing of the notice more than 1500 checks have been received from over a quarter of the Society's fellowship, some of the contributions being for sums in excess of that called for. Remarkably few direct refusals to contribute have been received; some of the fellows of the Society have expressed their desire to withhold their contributions until assurance can be given that the American Medical Association will use the fund wisely and constructively.

Under new business the spokesmen for a group of sincere and thoughtful younger fellows of the Society suggested certain constructive proposals that the Society might endorse and strongly recommend to the Association for its adoption. These proposals expressed a belief that the health of the people will be best served by medical care free of Government administration and control, and called attention to the profligate waste and duplication in health programs operated by the Government, as reported by the Hoover Commission. They indicated the belief of their proponents that the manner of expression of policy on the part of the American Medical Association has served to diminish public confidence in that body, and that its policy should be one of more active and enthusiastic support of constructive proposals for more equitable distribution of medical care. They further suggested endorsement by the Council of the principles for the distribution of medical care that were agreed upon by the Section on Medical Care of the National Health Assembly held in Washington in May, 1948.

These proposals were referred to a joint committee of the Committee on Public Relations and the Committee on Medical Economics.

The reports of the various committees were accepted and their recommendations in general were adopted; the recommendations of the Advisory Subcommittee on Malpractice Insurance regarding listeners at malpractice suits were, however, rejected.

AUREOMYCIN — ANOTHER EFFECTIVE ANTIBIOTIC

THE antibiotics that have proved most active or most promising for clinical use have come either from molds, like penicillin, from spore-forming bacilli, like gramicidin (tyrothricin), subtilin and bacitracin, or from actinomycetes of the genus Streptomyces. A concentration of interest in strains of the last genus was stimulated, of course, by the high activity and effectiveness of streptomycin. Another of the recent antibiotics derived from a species of Streptomyces was chloromycetin. Some of the unusual properties of this antibiotic — namely, its high degree of effectiveness against rickettsias and against certain of the large viruses as well as the in vitro susceptibility of both gram-negative and gram-positive organisms to that agent — have been referred to in these columns.[1]

A new antibiotic, aureomycin, that is derived from a species of soil organism, which has been named *Streptomyces aureofaciens*, has now been shown, on the basis of laboratory evidence and clinical trials, to give promise of being a useful addition in this field. The early reports presented at the New York Academy of Sciences last July[2] and additional papers that have already appeared[3-12] have indicated that aureomycin, like chloromycetin, should prove most useful against infections with all the known rickettsias and with the viruses of the

lymphogranuloma-venereum-psittacosis group. In addition, aureomycin has been shown to be of considerable, though more limited, therapeutic value in many infections with gram-positive and gram-negative bacteria. Like chloromycetin it has the advantage of being effective when used by mouth and is relatively nontoxic.

The exact field of usefulness, the toxicity and the limitations of this new antibiotic, however, are still to be worked out.

The paper by Finland, Collins and Wells in the present issue of the *Journal* and similar observations by other workers[13, 14] suggest that aureomycin may also be highly effective in the treatment of cases of primary atypical pneumonia, although the authors are quite cautious in the interpretation of their results. These findings, however, should stimulate further attempts to isolate and define the etiologic agent in this disease, which has become increasingly prominent as the seriousness of the bacterial pneumonias has been reduced by the use of the available chemotherapeutic and antibiotic agents.

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— WHAT THY RIGHT HAND DOETH

Something more than a generation ago universal custom demanded that the American school child write with the right hand, or else. A small army of potential scholars, during those unhappy years, had their slate pencils snatched from their southern paws by irate schoolmarms and were forced thereafter to lead lives of frustration, unlearned in spelling and stuttering in speech. Or so it later came to be believed, after the discovery of the specific language disability.

This later revelation of recent decades, while it disclosed the injustice that had been done to one group of embryonic citizens, set all to rights for the next. The pendulum that had reached the northernmost antipode of its excursion swung back upon its course and drove with equal vigor to the left. Since then it has been a foolhardy teacher indeed, or the most ignorant of parents, who would dare disturb the handedness with which heredity, chance, divine providence or a solemn design of inscrutable nature had endowed a child.

Why man, outwardly so symmetrical in his anatomic architecture, should exhibit such a stubborn bias in the unilateral development of his manual skills is interestingly discussed by Eustis elsewhere in this issue of the *Journal*. No one knows why the preferred hand is the right (a fact discernible on both sides of the equator), and no theory accounts satisfactorily for it. Right-handedness becomes most nearly universal as cultural development advances; primitive races show a higher percentage of left-handedness than do cultured races; 5 per cent of civilized adults are left-handed, 20 per cent of whom functioned in the counterclockwise direction during their kindergarten days.

The conclusion may be drawn that environmental pressure is highly important in determining ultimate handedness and that, unless inherent preference for the left is particularly strong, an artificially imposed shift to the right may not be the crime against humanity that it has so recently been considered. Ambidexterity introduces the really confusing factor. It is ambidextrous persons who sometimes know not which way to turn and whose left hands really know not what their right hands do, less certain in their abilities than the companies that rallied to David who "were armed with bows, and could use both the right hand and the left in hurling stones and shooting arrows out of a bow."

MASSACHUSETTS HEALTH CONFERENCE, INC.

An outstandingly progressive step toward the better distribution of medical care in Massachusetts was taken on November 28, 1948. On that date representatives of fifty or more "consumer" and "distribution" groups met together and organized the Massachusetts Health Conference, Inc.

First fruits of this organization consist of the Conference about to take place, on February 19 and 20, at the Hotel Statler, in Boston. Honorary chairman of the Conference is His Excellency, Governor Paul A. Dever; the chairman is Mr. Philip R. Mather, president of the National Health Conference. The president is Dr. John F. Conlin, director of medical information and education of the Massachusetts Medical Society, the vice-president is Mr. John J. Devlin, of the American Federation of Labor, and the secretary-treasurer is Mr. Louis T. Maloney, executive secretary of the Massachusetts Dental Society. The first Conference objective is "Means of Improving Health in Massachusetts during the Next Five Years."

It is a notable thing when members of diverse groups including both distributors and consumers sit down together to discuss their mutual problems, and a refreshing acknowledgment of the fact that most worthwhile objectives need to be viewed from various vantage points.

MASSACHUSETTS MEDICAL SOCIETY

TREASURER'S OFFICE

All members should be reminded that the proportion of the refund returned to each district society is based on the number of dues paid by March 1 in that district, and also that the names of members who have not paid their dues by March 1 are automatically removed from the mailing list of the *Journal* until such dues are paid. This year $8000 is being returned to the district societies.

Eliot Hubbard, Jr., *Treasurer*

BOSTON MEDICAL LIBRARY

Thanks to the loyal support of the members of the Massachusetts Medical Society the Boston Medical Library has been able to render greater service than ever before. During the past year 42,638 books and periodicals were made use of whereas the previous highest circulation had been 38,266 in any one year. Of considerable inter is the fact that over 9000 users of the Library we neither fellows, Society members nor membe This is the kind of service that should be rende and rendered gladly. It represents the same ty of service rendered by a free public library, whi must be paid for out of taxes. The added inco received from the Massachusetts Medical Soci members enables the Library to furnish this servi

The personnel of the Library has been increas and 1000 more periodical volumes have been pr pared and bound than during the previous ye The library has increased in size by over 29 volumes and 4000 pamphlets. It is still far fr its goal, but it is on its way.

The great need now is to obtain enough mon to complete the stacks so that valuable volum will be more readily available. This will cost ap proximately $75,000.

Next year the Boston Medical Library celebrate its seventy-fifth anniversary, and it is hoped tha it may be celebrated by dedicating the new stacks The members of the Massachusetts Medical Society can rightly take pride in their contribution t help support and carry on the work of this grea and valuable library.

Walter G. Phippen, *Presiden*

CORRESPONDENCE

COMMITTEE FOR THE NATION'S HEALTH

To the Editor: A bill has been introduced into the 81s Congress to develop a national health program. With th President strongly in its favor and the Congress compose as it is, there is a reasonable chance that such legislation wi be enacted into law. It is important, therefore, that th medical profession and others to whom Congress will turn for advice be so informed on the subject that clear thinking will result. Unfortunately, appreciable misinformatio regarding the subject has been broadcast throughout the country. A recent example is the inaugural address by Dr. William B. Rawls on assuming the presidency of the Medica Society of the County of New York. This address, which received publicity in the lay and medical press, contained many inaccurate statements and misleading innuendoes, and specifically mentioned me and the Committee for th Nation's Health, of which I have the honor to be chairman. I have corresponded with Dr. Rawls in the hope that h would be willing to correct these inaccuracies, but we have been unable to come to an agreement on the facts. We have left our correspondence with the understanding that I would present my point of view for the benefit of the physician and laymen. Naturally, I prefer to present the subject through the medical press, and therefore, I hope you will be willing to publish this letter in the *Journal*, which is th medium in which I should like to have any communication from me published.

In his address Dr. Rawls says, "One of the major weak nesses of Compulsory Health Insurance is that it makes no provision whatsoever for the care of those people who are not able to pay their own medical expenses." In all the proposed legislation so far supported by the Committee for the Nation's Health the medically indigent — namely, those provided for in part by Government or charity — will cease to be indigent and under the plan become the private patients of their own physicians. Furthermore, provision is made under the plans so that local communities can insure the really indigent for whom they must accept responsibility.

The address presents as evidence for Dr. Rawls's point of view the study of the status of medical care in the United States by the Brookings Institute without pointing out that

two experts in the field have filed an unchallenged criticism of this report with the Sub-committee on Health of the Senate Committee on Labor and Public Welfare.

The address says that compulsory health insurance will result in the socialization of medicine. At the present time we do not have compulsory health insurance, but we do have a great deal of socialized medicine as defined by General Paul R. Hawley, chief executive officer of the Blue Cross and Blue Shield Commission, who says, "Socialized medicine is medical care supported in whole or in large part by tax money and regulated by the government." Among good examples are the United States Public Health Service, the Veterans Administration, state universities and many tax-supported hospitals.

Dr. Rawls calls attention to the statement of Bernard M. Baruch, regarding the relation of doctors to Government: "I oppose socialization here. It leads ultimately to the police state, degradation of the individual and lessened well-being." No mention was made that in the same speech Mr. Baruch said, "Your organizations have been particularly active in pressing voluntary health insurance. . . . But I would not be frank — nor friendly — if I did not add what you know. It is not good enough." Mr. Baruch then went on in the same speech to propose compulsory health insurance. He declared: "Nationally, the program might well be administered by a body of doctors and non-doctors to keep medical care as free from politics as possible." This program, he pointed out, "can be devised, adequately safeguarded, without involving what has been termed 'socialized medicine.' "

Without specific reference the address stated that recent public-opinion polls have shown that compulsory health insurance is not the desire of the people. The following specific references on this subject are offered:

A statement by the National Opinion Research Center, University of Denver, in 1944, that "85 per cent thought social security should include doctor and hospital care."

A 1946 poll by the California Medical Association showed that 50 per cent of California residents favor some Government medical program.

A poll in 1946 in New York State under the direction of a Commission on Medical Care appointed by Governor Thomas E. Dewey showed that 84 per cent of New York State residents want health insurance.

Although the address did not specifically say that everyone who is in favor of what is loosely called socialized medicine is a Communist, appreciable space was given to the innuendo that those supporting compulsory health insurance are dominated by Communism. A survey of the individuals and groups supporting the compulsory health insurance program should make clear to any fair-minded person the absurdity of this innuendo: President Harry S. Truman, Jonathan Daniels, Russell Davenport, William Green, Bishop Francis J. McConnell, Philip Murray, Bishop G. Bromley Oxnam, Mrs. Franklin D. Roosevelt, David Sarnoff, Gerard Swope, Dr. Thomas Addis, Barry Bingham, Dr. Ernst P. Boas, Morris Llewellyn Cooke, John J. Corson, Mrs. Gardner Cowles, Michael M. Davis, Albert W. Dent, Abe Fortas, Mary Dublin Keyserling, Carl C. Lang, Mrs. Albert D. Lasker, Dr. John V. Lawrence, Dorothy Norman, Emil Rieve, Anna M. Rosenberg, V. Henry Rothschild, Second, R. M. Walls, D.D.S., and Matthew Woll. The program is also supported by six United States Senators, four of whom are members of a church that is irreconcilably opposed to Communism. Seventeen national organizations with memberships totaling some 18,000,000 persons endorsed nation-wide compulsory health insurance last spring at the National Health Assembly.

The address of Dr. Rawls declared that the conclusions of the Congressional Sub-committee on Publicity and Propaganda, often spoken of as the Harness Committee, have never been seriously denied. This committee claims that federal employees spent public funds improperly in furthering the cause of compulsory health insurance. The address did not mention that these charges have been referred to the Attorney General of the United States, and that he has up to the present time not seen fit to act upon them, which at least suggests that the charges of the Harness Committee cannot be substantiated.

The Tokyo Mission was cited as another instance of an attempt of Government employees to promote socialized medicine, the following quotation of the Harness Committee's Report being held as an example: "The real purpose of this Mission was to lay the groundwork for a system of socialized medicine in Japan and the scheme for such a Mission originated in the Division of Research and Statistics in the Social Security Board in Washington and nowhere else." Actually, it had been clearly demonstrated to this Senate Subcommittee that the Administration's health experts went to Japan at *the explicit request of General MacArthur and his staff*. In an official communication to Representative Harness, chairman of the committee that spread the false charge, MacArthur made clear that the request originated in his office, and that the purpose of the mission was to help reconstruct the national health insurance system, which had been instituted in that country by the Japanese in 1926.

The address said that Michael M. Davis, one of the principal founders and the most active member of the Committee for the Nation's Health was formerly an employee of the Social Security Administration. To correct this I call attention to the fact that Dr. Davis has never been a federal employee. Like many distinguished experts he has been asked by the Government to assist as a consultant from time to time. There is pay at $25.00 per day for a consultant. A consultant, however, is not an employee.

The address called attention to the fact that the Committee for the Nation's Health is registered with the Government as paid lobbyists. This is correct. If the implication in the address is that such activity is improper, it is only fair to call attention to the fact that the American Medical Association maintains a registered lobbyist in Washington and that the National Physicians Committee, closely allied to and approved by the American Medical Association, is also so registered, and further that its annual expenditures are ten times that of the Committee for the Nation's Health.

The address quotes from a report of the Canadian Royal Commission about the German plan of "political medicine" since 1884 as follows: "You will note the ever-expanding medical bureaucracy with its ever swelling tide of taxes and appropriations. After this process had been going on for fifty years, the whole arrangement was taken over lock, stock and barrel by Adolf Hitler, and the government's medical program was looked upon by many as one of the greatest props of the totalitarian state." Just what implication is meant from this quotation is not clear, but the address failed to mention that this same commission recommended Nation-wide Compulsory Health Insurance for Canada and that this recommendation was approved by the Canadian Medical Association. There are no obscure implications in these last two statements.

My hope is that the above corrections regarding fact and misleading innuendoes will permit members of a scientific profession to reach a decision about what type of national health program will be best.

CHANNING FROTHINGHAM, M.D.
101 Bay State Road
Boston 15

FAVORING THE ASSESSMENT

To the Editor: To those who object to the $25 assessment that we may have medical freedom, the answer can be given that indirectly they are paying Mr. Ewing far more per capita to secure their enslavement.

The assessment is a small amount, and all should cheerfully contribute that much and more, if able, in order to maintain our medical standards as they are and not to have directives from Washington.

JUSTUS G. HANSON, M.D.
218 Elm Street
Northampton, Massachusetts

BOOK REVIEW

Handbook for the Medical Secretary. By Miriam Bredow. Second edition. 8°, cloth, 389 pp., with 36 illustrations. New York: McGraw-Hill Book Company, Incorporated, 1948. $2.75.

This handbook, first published in 1943, has been revised, and the text brought up to date. A new section on secretarial duties in relation to veteran patients has been added to this edition. The whole field of office and patient management is covered, and there are special chapters on the preparation of manuscripts, the doctor and the law and the dental secretary.

The *World List of Scientific Periodicals*, which is not generally used to any great extent in the United States, is employed by the author instead of the abbreviations of the *Quarterly Cumulative Index Medicus* and the *Index Catalogue*, which are commonly used in this country. In the chapter on medical terminology there is a large vocabulary, comprising over 2000 medical terms, arranged by sixteen subjects. This list would have been more useful if all the terms had been arranged in one alphabet. The volume is well published. The work is intended as a student's textbook in teaching institutions, presenting courses for medical secretaries, office assistants and laboratory technicians. The book should prove useful also to all medical secretaries and should be in all medical libraries as a reference text.

NOTICES

NEW YORK STATE FELLOWSHIPS FOR TRAINING IN PUBLIC HEALTH

Fellowships to train physicians to qualify for public-health positions in New York State are available. The fellowships carry a stipend of $3,600 per year and are for one year or more, depending upon the training required. The types of training and qualifications are as follows: health officer, consisting of six or more months' supervised experience in a selected county or district health department followed by one academic year at an approved school of public health, leading to a degree of master of public health (applicant must be a citizen of the United States, graduate of an approved medical college, have an internship of one year in a hospital approved for such internship, be licensed or eligible to take the examination for license to practice in New York State and preferably should be no more than thirty-five years of age, although the age requirement may be waived); tuberculosis physician, consisting of three months in a tuberculosis hospital, nine months' supervised experience in tuberculosis clinics and two months' general public-health training in a selected district or county health department, with provision, if desired, for academic training, leading to a master of public health degree (applicant for this training must be a citizen of the United States, graduate of an approved medical college, have an internship of one year in a hospital approved for such internship, be licensed or eligible to take the examination for license to practice medicine in New York State and preferably should be no more than thirty-five years of age, although the age requirement may be waived); clinical consultant in venereal disease, in pediatrics, in obstetrics or in the administration of a specialized program such as cancer control requiring training in the clinical specialty concerned, as well as in general public health, for not more than two years to qualify for these specialty positions (applicant for this training must be a citizen of the United States, graduate of an approved medical college, licensed or eligible to take the examination for license to practice medicine in New York State and must have some experience in the clinical field for which he will be further trained); and laboratory director, consisting of one year of planned instruction in the New York State Health Department laboratory (applicant must be a citizen of the United States, licensed or eligible to take the examination for a license to practice medicine in New York State and must have had at least one year's laboratory training and experience).

Applications are invited by the New York State Department of Health. Further information and application forms may be obtained from Dr. Franklyn B. Amos, director of the Office of Professional Training, New York State Health Department, Governor Alfred E. Smith State Office Building, Albany 1, New York.

NEW ENGLAND CENTER HOSPITAL

The corporate name of the charitable corporation that operates the Joseph H. Pratt Diagnostic Hospital and the Ziskind Research Laboratories and will operate the new surgical hospital has been changed to New England Center Hospital. The individual units will continue to use their old names, but in referring to them as a group and also for certain formal purposes the new name will be used.

This is a change of name only and has no other significance or effect.

SUFFOLK CENSORS' MEETING

The censors of the Suffolk District Medical Society will meet for the examination of candidates at the Boston Medical Library, 8 Fenway, on Thursday, May 5, at 4 p.m.

CORNELL MEDICAL ALUMNI ASSOCIATION

The alumni day activities of Cornell University Medical College Alumni Association will be held on Thursday, March 24, at the College. The program will include lectures, a surgical program, research demonstrations, the annual meeting of the Association and an evening entertainment at the Waldorf-Astoria.

All Cornell medical graduates are urged to attend.

AMERICAN COLLEGE OF ALLERGISTS

The annual meeting of the American College of Allergists will be held at the Palmer House, Chicago, from April 14 to 17. The program will include a motion picture in color entitled "Bronchoscopy," a symposium entitled "Mold Fungi in the Etiology of Respiratory Allergic Diseases" and a discussion "Cottonseed Protein vs. Cottonseed Oil Sensitivity," as well as papers on other aspects of allergy and a panel discussion on "Pediatric Allergy." There will be more than twenty scientific and forty technical exhibits.

Members of the College and their wives, as well as non-members, are invited. Registration, free of charge, is required. Those attending the meeting are requested to make their own hotel reservations directly with the reservation manager, Palmer House, Chicago 90, Illinois.

AMERICAN ACADEMY OF GENERAL PRACTICE

The first annual scientific assembly of the American Academy of General Practice will be held at the Netherland Plaza Hotel, Cincinnati, March 7, 8 and 9. The following doctors will speak: Walter C. Alvarez, Rochester; M. Edward Davis, Chicago; Paul A. Davis, Akron; John E. Dees, Durham; Charles A. Doan, Columbus; Joseph A. Freiberg, Cincinnati; Lowell S. Goin, Los Angeles; Francis C. Grant, Philadelphia; Tinsley R. Harrison, Dallas; Robert A. Kehoe, Cincinnati; John A. Kolmer, Philadelphia; Karl A. Meyer, Chicago; Norman F. Miller, Ann Arbor; Francis D. Murphy, Milwaukee; Franklin D. Murphy, Kansas City; Walter J. Reich, Chicago; Howard A. Rusk, New York City; Tom D. Spies, Birmingham; Philip Thorek, Chicago; and Herman G. Weiskotten, Syracuse.

Scientific sessions will be held on all three days of the meeting. The program is a broad one, selected by general practitioners for general practitioners, and featuring topics of down-to-earth value to the man in general practice.

The Academy extends the invitation to attend to all members of the American Medical Association.

For reservations application should be made to Subcommittee on Hotels, American Academy of General Practice, 910 Dixie Terminal Building, Cincinnati 2, Ohio.

SOCIETY MEETINGS AND CONFERENCES

JANUARY 7–APRIL 13. American College of Surgeons. Sectional Meetings. Page xi, issue of December 23.

FEBRUARY 23. Norfolk District Medical Society. Page 240, issue of February 10.

FEBRUARY 25. Boston Surgical Society Page 240, issue of February 10.

FEBRUARY 28. Norfolk District Women's Auxiliary. Page 240, issue of February 10.

MARCH 7–9. American Academy of General Practice. Notice above.

MARCH 10. Evaluation of the Treatments of Arthritis. Dr. Walter Bauer. Pentucket Association of Physicians. 8:30 p.m. Haverhill.

MARCH 24. Cornell Medical Alumni Association. Notice above.

MARCH 28–APRIL 1. American College of Physicians. Page 158, issue of July 22.

APRIL 5–8. Postgraduate Institute of Philadelphia County Medical Society. Page 240, issue of February 10.

APRIL 14–17. American College of Allergists. Notice above.

MAY 4. New England Obstetrical and Gynecological Society. Springfield Country Club, Springfield.

MAY 5. Suffolk Censors' Meeting. Notice above.

(*Notices concluded on page xv*)